Contaminant Candidate List 3 Chemicals: Classification of the PCCL to CCL

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List of Abbreviations and Acronyms

<	Less than
≤	Less than or equal to
>	Greater than
≥	Greater than or equal to
µg	Microgram, one-millionth of a gram
µg/L	Micrograms per liter
ANN	Artificial Neural Network
ATSDR	Agency for Toxic Substances and Disease Registry
CART	Classification and Regression Tree
CASRN	Chemical abstract services registry number
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
CUS/IUR	Chemical update system/inventory update rule
DBP	Disinfection byproduct
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	United States Environmental Protection Agency
g/day	Grams per day
HRL	Health Reference Level
IOC	Inorganic compound
IRIS	Integrated Risk Information System
kg	Kilogram
L	Liter
LD_{50}	Lethal dose 50; an estimate of a single dose that is expected to cause the death of 50 percent of the exposed animals; it is derived from experimental data.
lbs	Pounds
LOAEL	Lowest observed adverse effect level
MARS	Multivariate Adaptive Regression Splines
MCMC	Markov Chain Monte Carlo
mg	Milligram, one-thousandth of a gram
mg/kg	Milligrams per kilogram body weight

mg/kg/day	Milligrams per kilogram body weight per day
mg/L	Milligrams per liter
N	Number of samples
NAWQA	National water quality assessment (USGS program)
NCOD	National contaminant occurrence database
ND	Not detected (or non-detect)
NDWAC	National Drinking Water Advisory Council
NIRS	National Inorganic and Radionuclide Survey
NOAEL	No observed adverse effect level
NRC	National Research Council
OW	Office of Water
OPP	Office of Pesticide Programs
PBPK	Physiologically Based Pharmacokinetic
PCCL	Preliminary-CCL
PWS	Public water system
QUEST	Quick, Unbiased, Efficient Statistical Tree
RTECs	Registry of Toxic Effects of Chemical Substances
RfD	Reference dose
TDS	Training data set
TRI	Toxics Release Inventory
UCMR	Unregulated Contaminant Monitoring Regulations
UCMR 1	First Unregulated Contaminant Monitoring Regulation
UCMR 2	Second Unregulated Contaminant Monitoring Regulation
UL	Tolerable upper intake level
US	United States of America
USGS	United States Geological Survey

1.0 INTRODUCTION TO THE CONTAMINANT CANDIDATE LIST (CCL) CLASSIFICATION PROCESS

The United States Environmental Protection Agency (EPA) developed a multi-step approach to select contaminants for the third CCL (CCL 3), which includes the following key steps:

(1) The identification of a broad universe of potential drinking water contaminants (CCL 3 Universe);

(2) A screening process that uses straightforward screening criteria, based on a contaminant's potential to occur in public water systems and thereby pose a potential public health concern, to narrow the universe of contaminants to a Preliminary-CCL (PCCL); and

(3) A structured classification process (e.g., a prototype classification algorithm model) that objectively compares data and information as a tool and is evaluated along with expert judgment to develop a CCL from the PCCL.

Steps 1 and 2 in the process are described in other support documents: *CCL 3 Chemicals: Identifying the Universe* (EPA, 2008a); and *CCL 3 Chemicals: Screening to a PCCL* (EPA, 2008b). The purpose of this document is to describe the methodology used to develop the classification process (Step 3) and the process used to select chemicals for the CCL 3.

The PCCL consisted of 532 chemicals that were screened from the CCL3 Universe. In order to select contaminants for the CCL 3, EPA used classification models to handle larger, more complex assortments of data in a consistent and reproducible manner. Learning from EPA's experience and expertise, the classification models were trained based on past expert decisions. The algorithms were used to prioritize chemicals which allowed the final expert evaluation and review to be more objective and efficient.

1.1 Principles of Evaluation

In developing the first CCL (CCL 1), the Agency utilized readily available occurrence and health effects information coupled with an expert review process. Following the publication of CCL 1, the Agency sought the advice of the National Research Council (NRC) and National Drinking Water Advisory Council (NDWAC). The panels provided recommendations to guide EPA in creating a more comprehensive and transparent evaluation of potential drinking water contaminants for developing future CCLs. In the light of the NRC and NDWAC recommendations, EPA has reviewed and evaluated a large number of contaminants and their data, developed decision making protocols using classification algorithm approaches, and included expert review in arriving at decisions to list or not list contaminants on CCL 3. These steps have provided a decision process that is more transparent and reproducible than approaches used for previous CCLs. The process is driven by the data on individual contaminants and minimizes the bias that may occur with expert panels due to the participants' individual

backgrounds and the confounding effects of group dynamics. As experience is gained, the new classification process is likely to evolve and improve for application to future CCLs.

To guide the development of the classification process, EPA identified several key features that the approach addresses.

1. Meaningful Basis for Classification. The classification process must reflect the critical goals of the CCL; that is, it must consider the potential for occurrence in water, the potential for causing adverse health effects, and it must prioritize contaminants based on these criteria. The data supporting the list no-list decision must be linked back to these three tenets.

2. Incorporating Relevant Data. The most relevant data used for the classification process include health effects data that are appropriate for drinking water exposures, and occurrence data that indicate the nature and spatial extent of potential occurrence in drinking water.

3. Transparent Process for Communication. One goal of the classification approach is to provide a transparent process that can be reviewed by external experts and the public. The attributes and data characterizing the contaminants should be easy to understand and the decision-making process to list or not list a particular contaminant must be conveyed in a straight forward manner.

4. Reproducibility. A key feature of the classification process is that it should be reproducible. The classification process should always give the same result for the same set of input information.

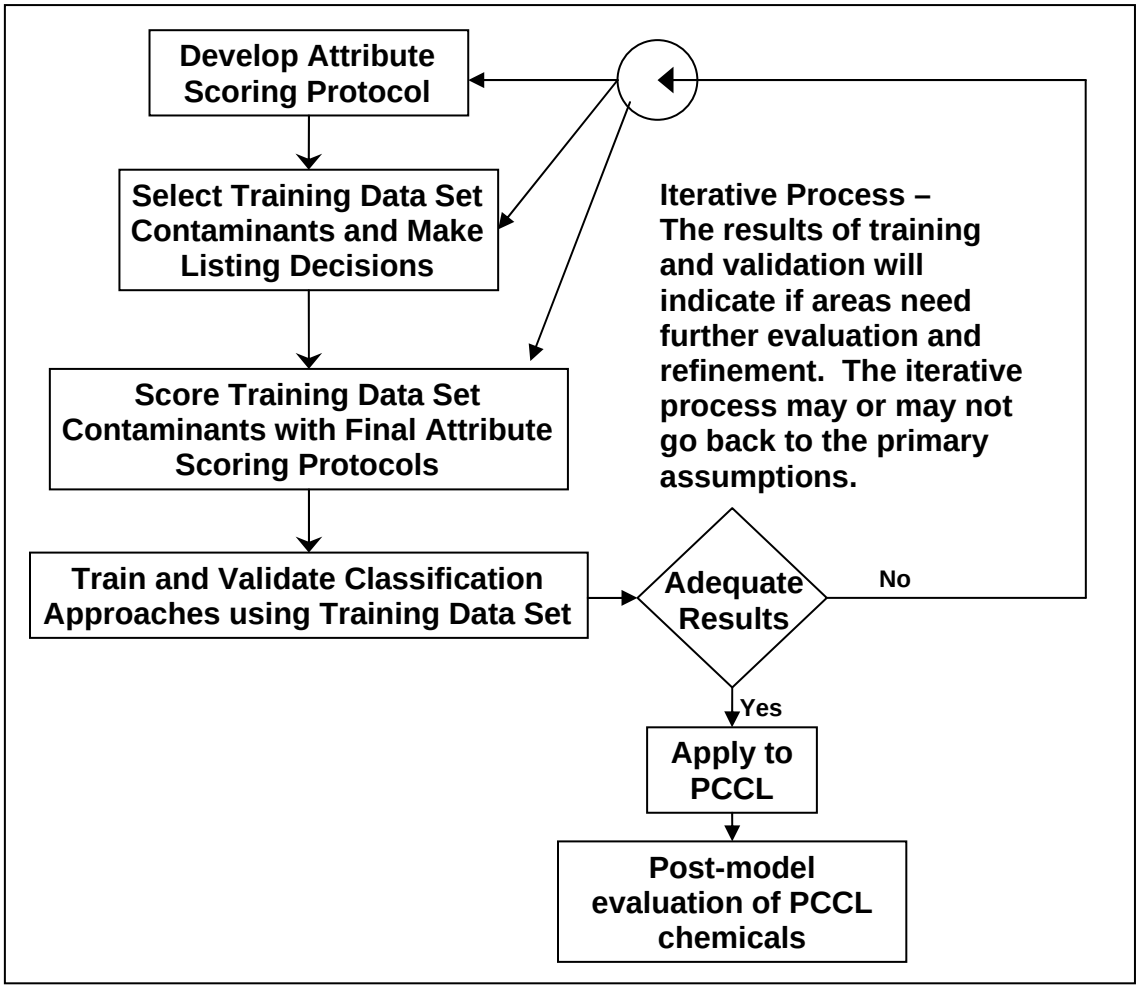
1.2 Developing the Classification Approach

Based on this framework, EPA developed an approach for classifying potential drinking water contaminants. An overarching premise in using classification models to prioritize contaminants is that different contaminants can be compared on the basis of similar attributes. The approach ensures that the contaminant attributes reflect the key decision characteristics in deciding whether or not to list a contaminant on the CCL. The attributes are properties used to categorize contaminants for their potential to occur in drinking water and for their potential to cause adverse health effects. For example, occurrence can be characterized by a contaminant's water concentration data or potential to occur based on its release to the environment. The adverse health effects of contaminants can be characterized using preliminary toxicological data such as median lethal dose (LD_{50}) or more developed values such as oral reference doses (RfDs). To evaluate, categorize, and prioritize the PCCL contaminants as potential CCL contaminants, EPA integrated various types of data that represent measures of their attributes. This relative assessment across data measures normalized the available data by developing a set of attribute scales for the attribute data, and scoring mechanisms for the various types of data available for potential drinking water contaminants.

Because of this new approach and its new application, EPA developed, tested, and evaluated the results of several classification algorithms to assess whether they are useful, and which ones

might provide the best decision support tools. To test and evaluate the process, EPA developed a data set and used it to "train" the classification algorithms. Once the modeling was completed, an Evaluation Team evaluated the model output based on the compilation of data for a subset of the modeled contaminants and assisted in developing a process to utilize the model output to generate the CCL 3. The following chapters describe the steps EPA used to develop the components of the classification process, as displayed in Exhibit 1.

Exhibit 1. Developing an Approach to Process PCCL Chemicals



Chapter 2 describes the attributes and scoring protocols. Chapter 3 describes the set of chemicals used to train the classification models, the training data set. Chapter 4 describes how the models were calibrated using the attributes and training data set. Chapter 5 describes the evaluation of the model output and post model processes.

2.0 ATTRIBUTES

Attributes are used to characterize different chemicals on the basis of similar qualities or traits. These qualities or traits represent the anticipated occurrence or adverse health effects of each contaminant. Occurrence and health effects are both represented by different types of data. To evaluate contaminants as potential CCL contaminants, one must be able to establish consistent relationships among the different types of data that represent measures of the attributes. This process involves the need to normalize the available data by developing scales and scoring mechanisms that will accept a variety of input data. The attributes are properties used to categorize contaminants for their potential to occur in drinking water and for their potential to cause adverse health effects. For example, occurrence may be characterized by water concentration data or a contaminant's potential to occur based on its release to the environment. The adverse health effects of contaminants may be characterized using preliminary toxicological data such as median lethal dose (LD_{50}) or more developed values such as oral reference doses.

The NRC recommended using the attributes Potency and Severity to describe health effects, and Prevalence and Magnitude to describe occurrence. When occurrence data are not available, they also suggested that environmental fate properties (i.e. Persistence and Mobility) could be used as surrogates to estimate potential for occurrence. The EPA workgroup agreed that the recommended attributes are appropriate and consistent with data used in the past decision-making efforts by EPA's Office of Water (OW).

Throughout the process of evaluating the attributes, it was recognized that a wide range of data elements would have to be used to characterize each attribute. The CCL process involves classifying relatively new and emerging contaminants and most will not have complete dossiers of data. If the same data were available for all chemicals their comparison and prioritization would be relatively straight forward. However, the types of data available for unregulated chemical contaminants varies. To enable comparisons among chemicals with differing types of data and information, a scaling system that accepts a variety of input data, yet provides a consistent comparative framework, is needed. In concert with NRC and NDWAC recommendations, EPA identified the following principles to guide development of the attribute scoring process:

- Attribute scores should increase with concern (e.g., a 10 is of greater concern, 1 of lesser concern);
- There should be sufficient scoring categories to capture the range of data and to discriminate among the data;
- The number of categories should not be so great that they create a false sense of precision;
- Attributes can use different numbers of scoring categories if necessary (i.e., Prevalence could use 1-10, while Severity could use 1-8);
- The possible range of the scores for a given attribute should be the same regardless of the data elements that are used to assign the score for that attribute;
- The data source and data element used for each attribute should consider more direct measures of occurrence or health effects before potential measures; peer reviewed data before unpublished data, and measured data before modeled data.

- The calibration scale (i.e., the scale relating the range for a data element to the scoring categories) should be established using a representative "universe" of data for each attribute to capture the potential range of values that might be encountered;
- The calibration scale must be set and remain constant throughout the operational process; and
- The scoring approach should be as simple as possible and data should be used with minimal transformations.

Section 2.1 describes the development of the process used to score the health effects attributes, and section 2.2, the approach for the occurrence attributes.

2.1 Health Effects Attributes

Potency and Severity are the two attributes used for evaluating health effects. As defined in detail below, Potency reflects the lowest dose of a chemical that causes an adverse health effect in a case study report or in a toxicological or epidemiological study. Severity is the adverse health effect associated with the dose that is used as the measure of Potency, and is calibrated based on the health-related significance of the adverse effect (e.g., dermatitis versus cancer). These two attributes are interrelated, in that the Severity is linked to the measure of Potency.

2.1.1 Potency

Potency is a value that indicates the power of a contaminant to cause adverse health effects. In the case of chemicals, that power is apparent in the dose required to cause the most sensitive manifestation of an adverse health effect, or to generate a particular excess cancer risk. Potency for chemicals is reflected in several standard toxicological parameters that are discussed below.

A number of approaches have the potential to be useful in scoring the Potency attribute. However, regardless of the approach selected, the methods require calibrating the scores to normalize the scale. To evaluate the data elements and establish consistent scales, an initial "learning set" of about two hundred chemicals was developed for use in experimentation with approaches to calibration. The chemicals considered included regulated chemicals and unregulated chemicals for which EPA has derived Health Advisories (EPA, 2004). These chemicals are primarily at the high end of the Potency scale. To ensure that the Potency scale covers the full range of conditions that may be encountered (from high to low Potency) in a universe of chemicals, a group of chemicals (nutrients/food additives) that are generally considered as relatively non-toxic and have toxicity values that can be compared to health advisories were added to the learning set.

The following toxicity parameters were compiled for the learning set chemicals, and their numeric distribution across the range of values was examined (see the footnotes below for definitions of the terms).

- Reference Dose (RfD)[1] or equivalent
- Cancer potency[2] (concentration in water equivalent to a 10^{-4} cancer risk)
- No Observed Adverse Effect Level (NOAEL)[3] and/or Lowest Observed Adverse Effect Level (LOAEL)[4] associated with the RfD
- Rat oral median Lethal Dose (LD_{50})[5] .

Several approaches to characterize the distribution of values for the different toxicity parameters were employed in this exercise. The approaches are described in the following section.

The data for the learning set were obtained from the following sources:

- EPA's Integrated Risk Information System (IRIS)
- EPA's Office of Water Health Advisories Documents[6]
- Registry of Toxic Effects of Chemical Substances (RTECS) (Mostly LD_{50} values)
- Tolerable Upper Intake Levels (ULs) from the Institute of Medicine Dietary Reference Intakes.

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[1] A Reference Dose (RfD) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It is expressed in mg/kg/day. The Agency for Toxic Substances and Disease Registry (ATSDR) lifetime Minimal Risk Levels (MRLs), World Health Organization (WHO) Tolerable Daily Intakes (TDIs), WHO and Food and Drug Administration (FDA) Acceptable Daily Intakes (ADIs), and the Institute of Medicine (IOM) nutrient Tolerable Upper Intake Levels (ULs) are roughly equivalent to the RfD.

[2] For this exercise cancer potency was evaluated as the concentration in drinking water equivalent to an excess cancer risk of one case in 10,000 (10^{-4}). This value is given in the Office of Water (OW) Drinking Water Standards and Health Advisories Tables and also is included in all Integrated Risk Information System (IRIS) Summary documents. When the 10^{-4} risk value is not available, it can be calculated from a cancer slope factor.

[3] NOAEL is a No-Observed-Adverse-Effect Level. It is the highest dose in a toxicological study or a group of studies that has no observed adverse effect.

[4] LOAEL is a Lowest-Observed-Adverse-Effect Level. It is the lowest dose in a toxicological study or a group of studies that causes an adverse health effect.

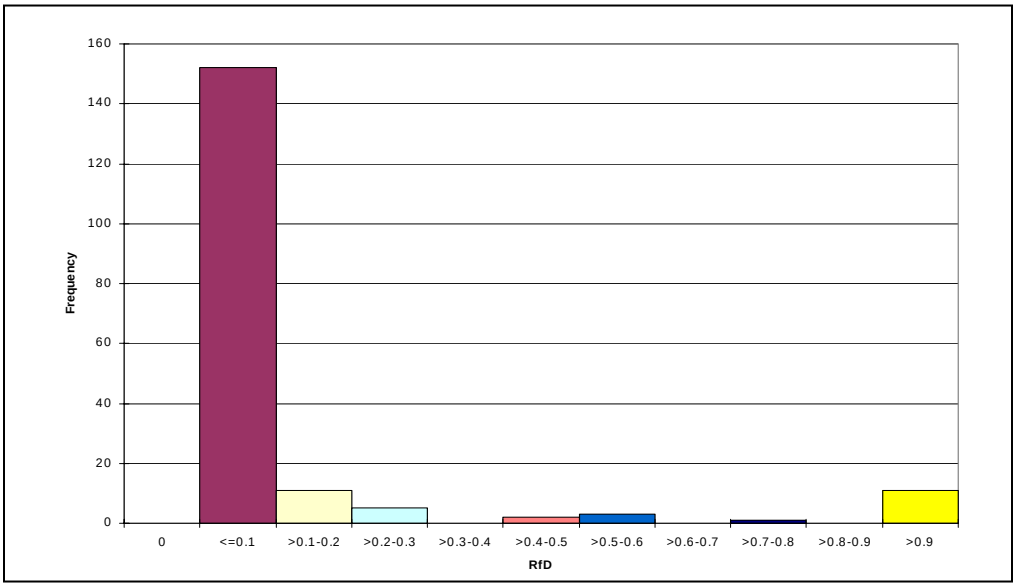
[5] An oral median Lethal Dose (LD_{50}) is an estimate of the oral dose that will cause the death of 50 percent of the exposed animals. LD_{50} data are based on acute exposures with limited post-exposure observations of the animals for cause of mortality, clinical signs, and gross pathology.

[6] The 2002 Edition of the Drinking Water Standards and Health Advisories was used for the RfD and 10^{-4} risk values.

2.1.1.1 Potency Data – Calibrating Scales and Scoring

Once the data for the learning set of chemicals was collected, they were arrayed and graphically displayed to analyze their range and distribution. For the initial evaluation, the range (in mg/kg/day) was divided into approximately ten equal units (deciles). This distribution was found to be highly skewed, with a large majority of the values falling in the decile of highest toxicity (see Exhibit 2 for an example). Two factors influenced this result. The first factor is that the range of values covered up to twelve orders of magnitude for the parameters evaluated. The second factor is that the set of contaminants contained both toxic chemicals as well as those generally regarded as safe (in keeping with the principles) and there are far more toxicological data available in the literature on chemicals considered to be toxic than for those, like the nutrients, that are only weakly toxic. This shifts the volume of data toward the chemicals with higher potencies. Most chemicals that are generally regarded as safe have limited available toxicological data, as their nutritional and commercial uses do not indicate a potential hazard at low to moderate intakes.

Exhibit 2. Decile Distribution of RfD Values



The second distribution evaluated was based on logarithms (base 10) of the toxicity parameters rounded to the nearest integer (see Exhibit 3A-D as examples).

Exhibit 3A. Logarithmic Distribution of RfD Values

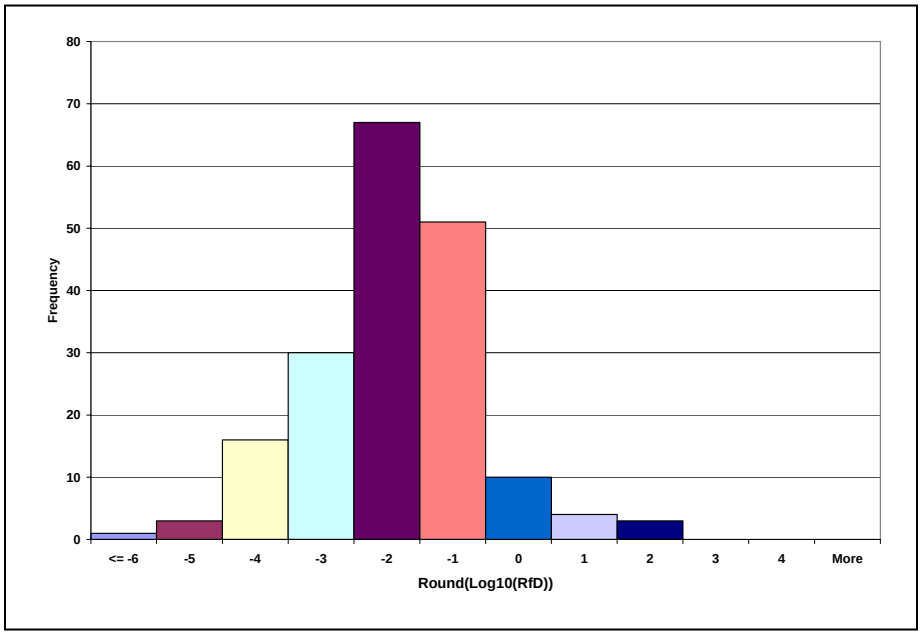


Exhibit 3B. Logarithmic Distribution of NOAEL Values

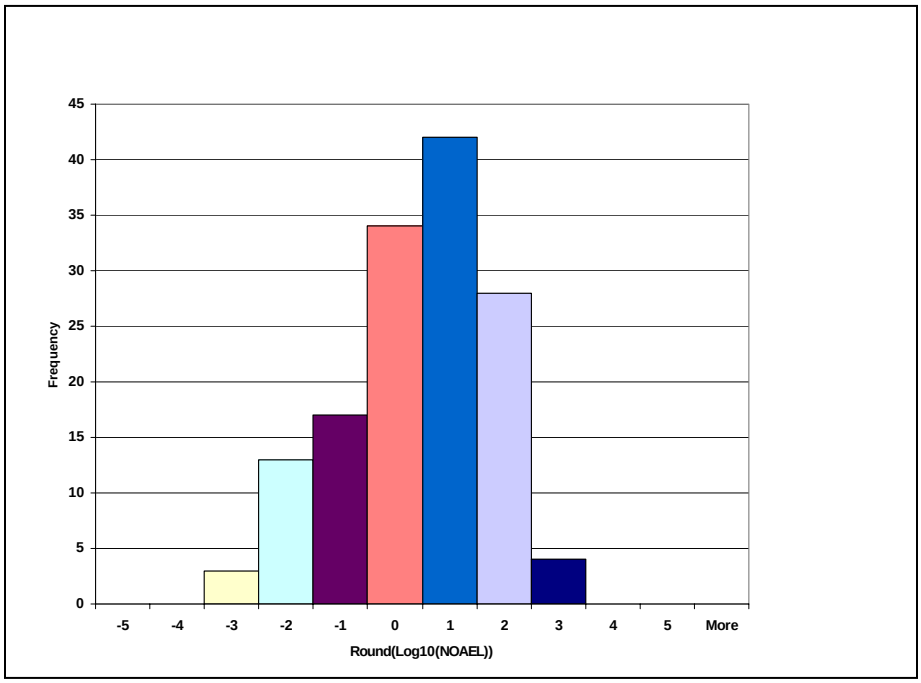


Exhibit 3C. Logarithmic Distribution of LOAEL Values

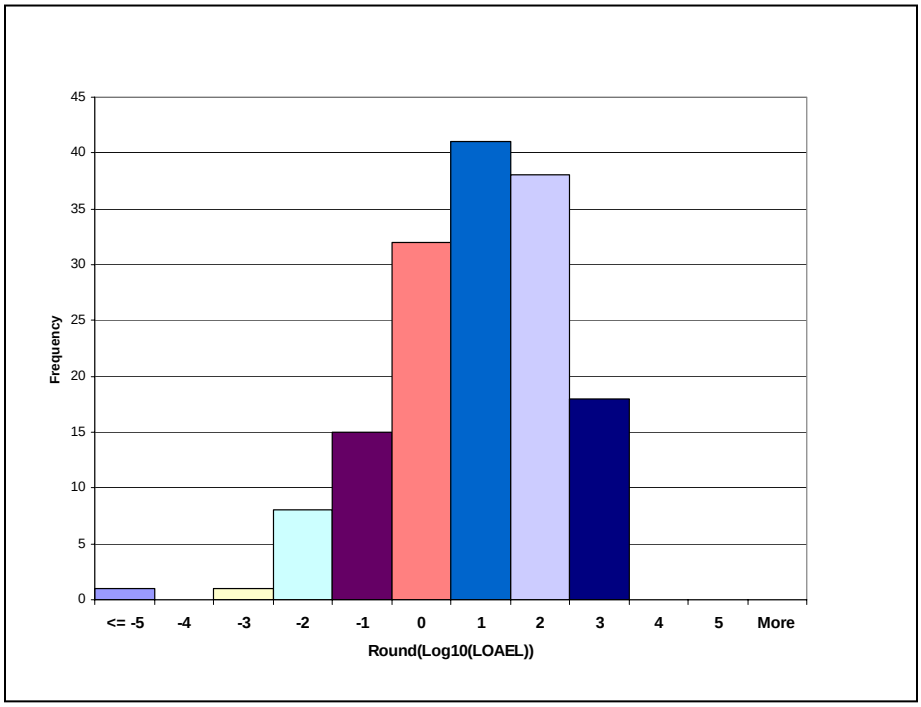
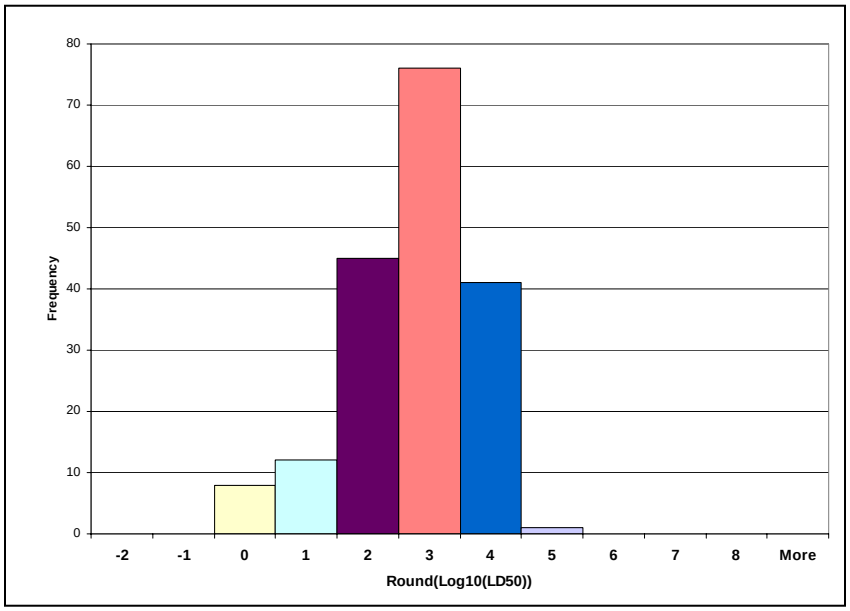


Exhibit 3D. Logarithmic Distribution of LD_{50} Values



The decile distribution (Exhibit 2) was found to be undesirable in developing a protocol for scoring Potency because almost all of the chemicals are clustered at one end of the distribution. This does not provide a good distribution of scores for discrimination of differences. With the decile distribution, almost all of the chemicals in the learning set would have a high Potency score of 10. Very few chemicals would have lower scores. The distribution based on the rounded Log_{10} of the toxicity parameter provided a distribution that spread the chemical toxicity parameters across the range and the most frequent Log_{10} value is approximately in the middle of the range making the curve roughly log-normal Exhibit 3A-D). It was for this reason that the Log_{10} distribution was selected for development of the scoring equation. The distribution of toxicity values is still somewhat skewed toward higher toxicity scores; however, this is a product of limited available data for the weakly toxic chemicals.

The log-based distribution was used to establish a scoring equation for Potency for each measure of toxicity. This was accomplished by assigning the most frequent (modal) value in the distribution a score of 5 on a 10 point scale and solving an equation for each type of toxicity parameter that would make that distributional value equal a score of 5. For example, in Exhibit 3A (RfD), the most frequent value is a rounded logarithm of -2 (0.01). The scoring equation for the RfD values was developed as follows:

5 = 10 - (most frequent rounded log + X)
5 = 10 - (-2 + X)
5 = 10 + 2 -X
5 = 12 - X
5 - 12 = -X
-7 = - X
7 = X

Accordingly the equation for scoring the RfD values is

Score = 10 - (rounded log of RfD + 7)

The scoring equations for the other measures of toxicity were derived from the modal rounded logarithm values of their distributions in a similar fashion. As displayed in Exhibit 3, the position of the modal rounded log differed for the different measures of toxicity, which necessitated differing equations. The resultant equations are summarized in Exhibit 4.

Exhibit 4. Scoring Equations for Potency
RfD Score = 10 - (Log_{10} of RfD + 7)
NOAEL Score = 10 - (Log_{10} of NOAEL + 4)
LOAEL Score = 10 - (Log_{10} of LOAEL + 4)
LD_{50} Score = 10 - (Log_{10} of LD_{50} + 2)
10^{-4} cancer risk [1] Score = 10 - (Log_{10} of the 10^{-4} cancer risk + 6)
[1.] The concentration in water for 10^{-4} cancer risk in water was selected as the measure of potency for carcinogens because this is the value given in the Standards and Drinking Water Health Advisories Tables prepared by OW and also is provided in IRIS Summaries. Changing the reference value to the 10^{-6} risk would merely shift the rounded log value and the constant by two integers but would not change the score. Scores were restricted to whole number values with a maximum of 10 and a minimum of 1.

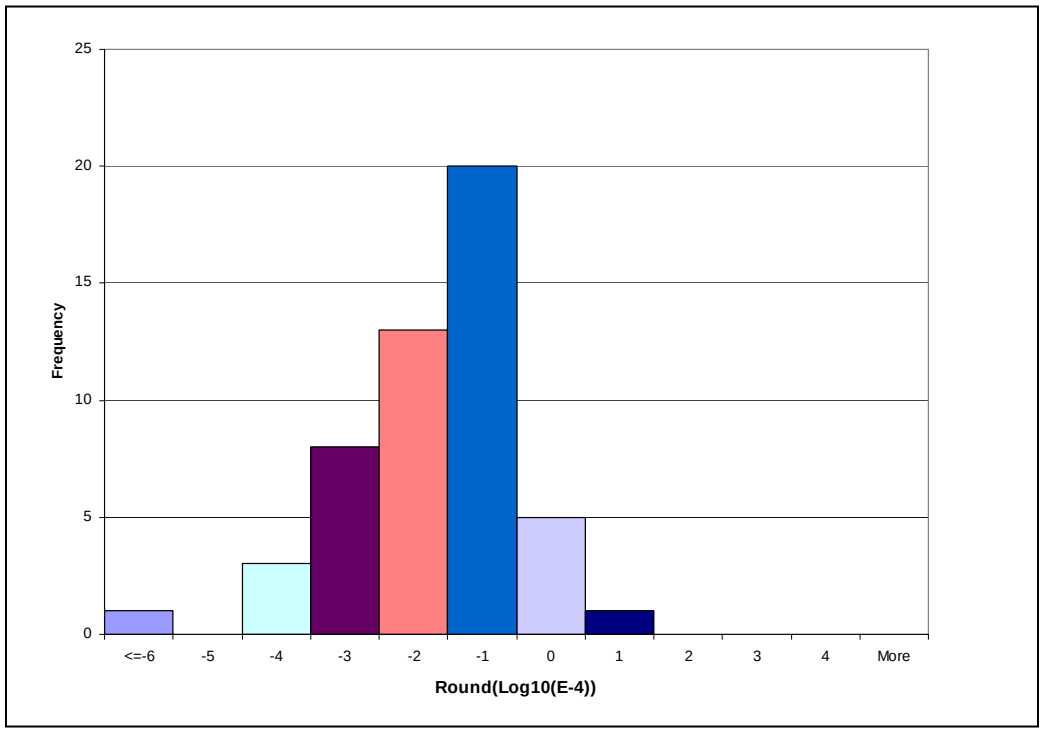
Some distributions for toxicity parameters span a range greater than ten orders of magnitude. EPA decided that calculated scores less than 1 would be given scores of 1 and calculated scores greater than 10 would be given scores of 10, which combine the chemicals at the tails of the distributions. Conversely, for the distributions that covered less than 10 orders of magnitude, no attempt was made to normalize the scores across a range of ten because the learning set is limited and could have been expanded by searching for chemicals that are more toxic than the most toxic substance in the learning set (dioxin with an RfD of 1 x 10^{-9} mg/kg/day) and less toxic than the least toxic chemical in the learning set (phosphorous with an RfD-equivalent of 57 mg/kg/day derived from the Institute of Medicine (IOM) UL. However an adjustment was made to accommodate LD_{50} values that are reported as greater than a specific numerical dose. In such a case, the highest dose used in the study did not cause death in 50 percent of the tested animals, indicating that the chemical is less toxic than would be indicated by the highest dose tested. Accordingly, the LD_{50} equation was modified to accommodate this situation and became:

$$LD_{50}\ \text{Score} = 10 - (\text{Log}_{10}\ \text{of} > LD_{50} + 3)$$

This change to the LD_{50} equation decreases the Potency score from that derived from the numeric value of the LD_{50} by one to accommodate the "greater than" designation. A similar adjustment was made for situations where the NOAEL in a critical study was the highest dose tested.

The distribution for cancer effects is the most skewed of those examined (see Exhibit 5). There are a greater number of chemicals that are more potent carcinogens when compared to those in the modal grouping than there are those that are less potent. This is not unusual because cancer bioassays are costly and there is an incentive to invest resources in studying chemicals that have a high likelihood of being potent carcinogens. No attempt was made to further normalize the cancer scores across a range of 10. For the chemicals in the learning set, the lowest cancer Potency score is 3.

Exhibit 5. Logarithmic Distribution of Cancer Potency Values



2.1.1.2 Evaluation of the Potency Scoring Protocol

All of the chemicals in the learning set were scored for each toxicity parameter to examine the consistency across scores for the non-cancer measures of Potency. Some examples of this evaluation are provided in Exhibit 6. Since the mechanisms that lead to the development of cancer involve some biological responses that are unique to tumors, the 10^{-4} cancer risk values were not included in this comparison. The scores for individual chemicals were compared across the toxicity values, and the agreement between scores was evaluated.

Exhibit 6. Potency Scores for Chemicals in the Learning Set				
Chemical	**RfD**	**NOAEL**	**LOAEL**	**LD_{50}**
Calcium (Calcium chloride for LD_{50})	1	ND	4	5
Cyanazine	6	6	6	6
Dioxin (2,3,7,8-TCDD)	10	ND	10	4
Hexazinone	4	5	4	5
Iodine (Sodium iodide for LD_{50})	5	8	8	4
Methyl ethyl ketone	3	3	3	5
Methyl parathion	7	8	7	7
Naphthalene	5	4	4	5
Phenol	4	4	4	5
Vitamin D	6	9	9	ND
ND = No data				

In addition, the scoring equations were applied to selected chemicals that were not in the learning set using data available in the Agency of Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles. Those results are summarized in Exhibit 7. The scores were evaluated for consistency across parameters.

Exhibit 7. Potency Scores for Chemicals Not in the Learning Set				
Chemical/ Potency Scores	**RfD-equivalent (mg/kg/day)**	**NOAEL (mg/kg/day)**	**LOAEL (mg/kg/day)**	**LD_{50} (mg/kg)**
Acrylonitrile	4	5	5	6
Ethion	6	7	6	6
Malathion	5	6	5	5
Endosulfan	6	7	ND	5
ND = No Data				

The agreement of non-cancer scores across the RfD, NOAEL, LOAEL and LD_{50} inputs was evaluated. There were 216 chemicals in the learning set; 13.5 percent of those with multiple non-cancer scores had identical scores across all parameters (see cyanazine in Exhibit 6). For 54.6 percent, the scores deviated by 1 integer (see hexazinone in Exhibit 6); 20.5 percent deviated by 2 integers (see methyl ethyl ketone in Exhibit 6). There was a 3-integer deviation for only 9.7 percent, and the majority of those were inorganic compounds (see iodine [sodium iodide] in Exhibit 6). Only 1.6 percent deviated by more than 3 integers (see dioxin in Exhibit 6). Scores deviated by two integers or less for 88.6 percent of the chemicals. The difference between scores

for a given compound was greatest for the relatively non-toxic chemicals. In almost all cases the NOAEL and LOAEL scores were higher than the RfD score, effectively negating the concerns that the inclusion of uncertainty factors in the calculation of the RfD would inflate the Potency score. For those chemicals with low uncertainty factors the NOAEL or LOAEL scores were often 3 or more integers higher than the RfD scores (see calcium chloride and vitamin D in Exhibit 6).

Since most chemicals with RfD values are also likely to have NOAEL, LOAEL, and/or LD_{50} values, a policy decision was needed with regard to how one should select the parameter used to score for a non-cancer endpoint. Since there is a general consistency among scores, the EPA workgroup determined that a hierarchy of RfD> NOAEL> LOAEL> LD_{50} would be used. In cases where a NOAEL is higher than the lowest LOAEL, the LOAEL would be used in its place. This hierarchy gives preference to the Potency value with the richest supporting data set (the RfD-or equivalent values) and the lowest ranking to the LD_{50} because it is a measure of acute rather than chronic toxicity. When comparing cancer and non-cancer scores, it was determined that the end point (cancer or non-cancer) that provided the highest measure of Potency would be used to score the candidate.

These evaluations were used to develop the scales and hierarchy of data used in the Potency Scoring Protocol, which is presented in Appendix A.

2.1.2 Severity

Severity refers to the relative impact of an adverse physiological change caused by a xenobiotic chemical in humans or animals on the ability of the human or animal to function and survive in the environment. The sixteenth century physician, Paracelsus, provided the underlying principle for the toxicological sciences with the axiom "the dose makes the poison." Just as toxicity increases with dose, so too does the Severity of the observed effect, in most cases. A low dose effect could be a simple increase in liver weight while the same chemical at a higher dose could cause cirrhosis of the liver. For that reason, the measure of Severity that will be used for scoring in the CCL process is the effect or effects seen at the LOAEL. Restricting Severity scores to the effects occurring at the LOAEL ties them to the data used to derive the Potency score – the type of data likely to be available for CCL candidates. This approach is consistent with the advice provided by the NRC and NDWAC (NRC 2001, NDWAC 2004).

The Severity measures that will be used for CCL scoring differ from those used for Potency, Prevalence, and Magnitude because they are descriptive rather than quantitative. Accordingly, they are less amenable to automation and often require more scientific judgment in their application. The sections that follow describe the approach that was used to derive the scoring protocol for Severity and to evaluate its performance.

2.1.2.1 Severity – Scales and Scoring

In developing the protocol for scoring Severity, the workgroup began with the system used by the NRC (2001) for their case study on methods for selecting a CCL from a PCCL. The NRC Severity scoring protocol was based on the anticipated clinical impact of the most sensitive endpoint in affected individuals. The NRC prototype for scoring Severity is provided in Exhibit 8.

Exhibit 8. NRC Severity Scoring Proposal	
Score	**Description**
0	No effect
1	Changes in organ weights with minimal clinical significance
2	Biochemical changes with minimal clinical significance
3	Pathology of minimum clinical importance (e.g., fluorosis, warts, common cold)
4	Cellular changes that could lead to disease; minimum functional change
5	Significant functional changes that are reversible (e.g., diarrhea)
6	Irreversible changes; treatable disease
7	Single organ system pathology and function loss
8	Multiple organ system pathology and function loss
9	Disease likely leading to death
10	Death

In trying to apply the NRC Severity prototype using the critical effects from EPA IRIS Health Risk Assessments, EPA toxicologists encountered difficulty because of the clinical components of the prototype. It was difficult to determine clinical outcomes such as function loss, treatability, or potential for mortality from the critical effects identified in IRIS. In addition, some of the features of a clinical progression could be influenced by the availability and affordability of treatment. The workgroup decided that it would not be appropriate to use a scoring scheme that had economic and environmental justice implications.

The critical effect data for PCCL contaminants will, in most cases, be expressed using terminology very similar to the terminology found in the IRIS database. Accordingly, critical effects of 100 IRIS chemicals were compiled and grouped into categories by EPA toxicologists. These categories were, in turn, used to build a scoring scale that applied some of the rationale reflected in the NRC prototype, but utilized the critical effects information most likely to be available from databases such as IRIS, which eliminated outcome judgments that would confound the scoring process. In this exercise, some difficulties were encountered in scoring Severity, particularly with assigning the middle score categories (3, 4, 5, and 6) and with classifying different types of cancer. Accordingly, the scoring protocol was modified again to try to provide better discrimination between the effects associated with the middle scores and remove the medical treatment considerations. Two new scoring options were developed. One was a nine-point scheme and the other a five-point scheme.

Testing of the two new scoring schemes was conducted by EPA toxicologists in the Health and Ecological Criteria Division of the Office of Water. Each toxicologist was presented with all the critical effects given in IRIS with no knowledge of the chemical or chemicals to which they were attached and the revised scoring protocols. They were asked to independently score the large group of critical effect descriptions. The toxicologists met as a group to compare scores and reach consensus on the score and category that is best suited for each critical effect. The five-point scale was compared to the nine-point scale. After completion of this exercise, the nine-point scale displayed in Exhibit 9 was selected based on its ease of use, more transparent clustering of effects within scoring categories, and consistency across the individual scores assigned by toxicologists.

Exhibit 9. Final Nine-Point Scoring Protocol for Severity		
Score	**Critical Effect**	**Interpretation**
1	No adverse effect	---------
2	Cosmetic effects	Considers those effects that alter the appearance of the body without affecting structure or functions
3	Reversible effects; differences in organ weights, body weights or changes in biochemical parameters with minimal clinical significance	Transient, adaptive effects
4	Cellular/physiological changes that could lead to disorders (risk factors or precursor effects)	Considers cellular/physiological changes in the body that are used as indicators of possible adverse systemic damage
5	Significant functional changes that are reversible or permanent changes of minimal toxicological significance.	Considers those disorders in which the removal of chemical exposure will restore health back to prior condition
6	Significant, irreversible, non-lethal conditions or disorders	Considers those disorders that persist for over a long period of time but do not lead to death
7	Developmental or reproductive effects leading to major dysfunction	Considers those chemicals that cause developmental effects or that impact the ability of a population to reproduce
8	Tumors or disorders likely leading to death	Considers chemical exposures that result in a fatal disorder and all types of tumors
9	Death	

The consensus judgment of the EPA toxicologists was used to construct a compendium of nearly 250 critical effect descriptions grouped by their severity scores (e.g., "Chronic irritation without histopathology changes" equals a score of 3). The final Severity protocol and compendium of critical effects are provided in Appendix A.

The ordering of the nine-point scale, which clusters developmental and reproductive effects at a score of 7, and assigns tumors or disorders likely leading to death a score of 8 became a point of discussion. Some reviewers of the protocol felt that a separation of developmental and reproductive effects by the seriousness of the outcome was better than the clustered approach. This option was discussed during internal review of model outcomes (Chapter 4) by the Agency workgroup. The Agency reviewers decided that the benefits of the proposed scale outweighed potential drawbacks. The ability to clearly identify PCCL chemicals with even a slight developmental reproductive or tumorigenic effect through their Severity score is benefit of the Exhibit 9 scoring system.

The scale's "uneven steps" were also noted as a point of concern. A detailed exploration of alternative options, which included the collapse or reordering of the categories resulted in a consensus judgment to retain the current scale. The current Severity scale works well in providing a meaningful categorization of the array of critical effects. Given the range of critical effects that result from a given exposure, it is not possible to have a consistent difference in the Severity of the outcome between each step on the scale.

2.1.2.2 Evaluation of the Severity Scoring Protocol

The Severity scoring protocol was evaluated using the group of chemicals that were included in the training data set discussed in Chapter 3 of this report. Evaluation criteria included:

- Ease of scoring using the protocol and critical effect compendium
- Correlation of the list or not list decisions made by workgroup members using the written narrative descriptions of the critical effects with those made with the numeric scores.
- Outcomes from the algorithm list/no-list decisions (discussed in Chapter 4) using the scored data as compared with workgroup's decisions based on the descriptive data.

During the initial evaluation process several issues were identified. The most challenging issue related to Severity scores derived from LD_{50} Potency data. According to the scoring protocol, the Severity score for an LD_{50} Potency value would be based on the outcome of death in the test population and result in a Severity score of 9. The same score of 9 would be given to a LOAEL or RfD from a more chronic study where the critical effect was described as decreased survival or longevity. When the evaluator's decisions based on descriptive information for both the Potency and Severity were compared to the decisions based on scores, it was apparent that the evaluators looked at the two effects differently. A decrease in survival from a standard chronic study was regarded as a more serious concern than death in a LD_{50} study where death is the targeted outcome. Several options were considered for solving this problem. The simplest option was to have no Severity score for an LD_{50} based Potency value. Another option was to retrieve the study that was the basis of the LD_{50} value and use the critical effect and dose for systemic effects observed rather than death. The last option was to look for a Potency value and critical effect from a toxicity study other than an LD_{50} study.

Experimentation with the three options for Severity based on LD_{50} values demonstrated that a combination of the second and third options provided a feasible alternative to scoring Severity on the basis of death when the Potency value was an LD_{50}. The option of eliminating the Severity score for an LD_{50} value was determined to be a poor choice since it fails to make full use of the available data. It was decided that only when attempts failed to identify an alternate study and/or pre-mortality effects in the LD_{50} study, that an LD_{50} based score of 9 would be assigned.

A problem was encountered with critical effect information for LOAELs from the RTECS database. This database summarized all effects without specifying which one was the critical effect. In cases where the original data source was available in the supplemental data, it was consulted to identify which effect was critical. When the supplemental data identified a NOAEL for the critical study it replaced the RTECS LOAEL. If the original source could not be accessed, an alternative NOAEL or LOAEL and its critical effect(s) were identified from the supplemental data and replaced the RTECS LOAEL. Two guidelines were applied when choosing the

replacement option. In most cases a replacement was made only if the new LOAEL was lower than the RTECS value. However, in some cases the alternate value, although greater than the RTECS LOAEL was chosen because it was from a study that was higher in quality, more accessible and more recent than the RTECS citation. .In any case where the RTECS remained the only source for the data, the score for Severity was based on the most serious of the cluster of effects presented.

Some problems with scoring were encountered in cases where critical effects were not included in the critical effect compendium. The compendium of critical effects descriptors was developed to allow people who were not toxicologists to score chemicals based on Severity. In cases where the scorers could not determine a Severity score, the data were submitted to EPA toxicologists. A minimum of three toxicologists scored the critical effect. The consensus score was determined and the critical effect descriptor and its score were added to the critical effect compendium.

One Severity scoring factor that may have had an effect on the correlation between the classification algorithm-based list/no-list decisions (See Chapter 4) and the workgroup decisions for the Training Data Set was the numeric Severity score of 8 for carcinogens. The only critical effect to score 8 was carcinogenicity. Workgroup members could easily identify carcinogens by their Severity score and possibly placed more emphasis on this result than the other numeric scores. The classification algorithm was less able to do so, particularly for carcinogens with low Potency values. For example, in some cases, the algorithm made a "no-list" decision when the Severity Score was 8 and the expert evaluators made a "list" decision primarily because of the Severity score's linkage to cancer. This was particularly true in a couple of cases where all the other scored values were identical or close to identical but Severity was a 7 compared to an 8 (cancer). The decisions for the algorithm and the workgroup matched more closely when Severity was a 7 than when it was an 8 with the workgroup more likely to choose a list decision for the 8 Severity score than the algorithm.

In most cases, the combination of Potency and Severity scores performed well in the workgroup exercises used in developing the PCCL to CCL process and the algorithm trials that followed (Chapter 4). Alternative approaches were adopted for dealing with LD_{50} based Potency values, and critical effect terms that were not initially in the critical effects compendium were added. Finding an alternative to an LD_{50} Severity score of 9 and consulting supplemental sources for critical effect information increased the effort required to obtain the Severity data, but appeared to function well. These changes are reflected in the Severity Scoring Protocol and Compendium of Critical Effects in Appendix A.

2.2 Occurrence Attributes

The attributes selected to define actual or potential occurrence of contaminants in drinking water are Prevalence and Magnitude. Magnitude is related to the quantity (e.g., concentration) of a contaminant that may be in the environment. Prevalence provides a measure of how widespread the occurrence of the contaminant is in the environment. When direct occurrence data are not available, Persistence and Mobility data are used as surrogate indicators of potential occurrence of a contaminant. Persistence-Mobility is defined by chemical properties that measure or estimate environmental fate characteristics of a contaminant and affect their likelihood to occur in the water environment.

Similar to the health effects attributes, the occurrence attributes are interrelated. The data sources and the learning sets used to define and scale Magnitude, Prevalence, and Persistence-Mobility, as well as more details about the individual attributes are described in the following sections. Unlike the health effects attributes, the data elements used to characterize occurrence are not solely based on a disciplined progressive study of the contaminants. The availability of data from surveys of contaminants in ambient and drinking water, the detection limits of analytical methods, limitations in reporting requirements, as well as indirect measures of potential occurrence needed to be considered and evaluated. Data sources that could provide occurrence data ranged from direct measures of concentrations in water to annual measures of environmental release or production.

The most relevant data for characterizing demonstrated occurrence are monitoring studies or surveys designed to assess national occurrence in drinking water. Finished drinking water occurrence data sources that have been compiled include the Unregulated Contaminant Monitoring Regulations (UCMR), the National Drinking Water Contaminant Occurrence Database (NCOD) (Round 1 and Round 2 unregulated contaminant data), and the National Inorganic and Radionuclide Survey (NIRS).

Finished water occurrence data are often not available for many chemicals, therefore other types of data that provide the measures of potential occurrence in Public water systems (PWSs) need to be considered. The workgroup identified national monitoring studies of occurrence in ambient waters, which may be the eventual source waters for drinking water supplies. Two US Geological Survey (USGS) data sources provide information on source water occurrence for CCL: the National Water Quality Assessment Program (NAWQA), and studies related to the National Reconnaissance of Emerging Contaminants. These sources provide direct measures of occurrence in potential source water and indicate possible occurrence in PWSs.

Many of the chemicals evaluated through the CCL process will not have direct water measurements (finished or ambient). Other available sources that provide data about the potential for drinking water occurrence include:

- the EPA Toxics Release Inventory (TRI), that reports annual volumes of chemicals released from industrial applications and the number of states in which those releases occur;
- the National Center for Food and Agricultural Policy's National Pesticide Use Database that provides estimates of the amount of pesticide applied and the number of states in which it is applied; and
- EPA's Chemical Update System/Inventory Update Rule (CUS/IUR), a source for annual production volume data under the Toxic Substances Control Act. Note the CUS/IUR data are categorical (i.e., chemicals are in categories with a range of production values, such as 500,000 to 1,000,000 pounds).

2.2.1 Prevalence and Magnitude Data Elements

A learning data set of 207 chemicals was compiled and used to develop and calibrate scales for scoring the Magnitude and Prevalence attributes. Due to the linkage of the data used, the scaling and scoring evaluations were performed concurrently. The linkage between Magnitude and Prevalence measures is shown in Exhibit 10. The Magnitude measure indicates the median

concentration of detections in water or the total pounds of the chemical released into the environment. The median was selected over mean because it typically is a more stable estimate of central tendency in environmental occurrence data. Outliers have strong influence on means, often to the extent that the mean is greater than all but the maximum value (particularly when only detections are used in the calculation). The median of detections was selected over the median of all measurements in water because all measurements would include non-detections. Non-detections either signify that the chemical is not occurring or the analytical method is unable to measure the chemical below the detection limit. The inclusion of non-detections reduces the median value and for the majority of environmental chemicals the median would be a less than value (i.e., < the reporting or a "non-detect" value). This would provide little information and limited discrimination among the chemicals. Prevalence uses the same data source as Magnitude. The linked Prevalence measure provides an indicator of how widely the contaminant may be present; in general Prevalence shows the proportion of monitoring sites or states with detections or releases.

Exhibit 10. Relationship of Data Elements Used to Score Magnitude and Prevalence.

Magnitude Data	Prevalence Data
Median concentration of detections from finished water systems.	Percent of finished water systems nationally with detections of a contaminant.
Median concentration of detections from ambient water sites.	Percent of ambient water sites nationally with detections of a contaminant.
Amount of total releases nationally in TRI; annual, in pounds.	Number of states reporting releases of the chemical in the Toxics Release Inventory.

Sections 2.2.2 and 2.2.3 discuss the approach used to develop and calibrate the scales for scoring Prevalence, and Section 2.2.4 through 2.2.7, discuss the approach for Magnitude including the use of Persistence and Mobility Scores as a surrogate for Magnitude when Production volume is used for Prevalence.

2.2.2 Prevalence - Calibrating Scales and Scoring

Prevalence is a measure of a contaminant's occurrence across the United States. It uses measures such as:

- Contaminant detections from Drinking Water Monitoring Programs
- Contaminant detections from Ambient Water Monitoring
- States where pesticides are applied
- States reporting releases of a given chemical to the environment
- Production of commodity chemicals in pounds per year.

These Prevalence measures have finite ranges such as zero to 100 percent of PWSs or 1 to 50 states depending on the reporting requirements of the available data source. Accordingly, transformations to log-based distributions are not necessary. The scaling analyses for Prevalence focused on establishing groupings of the chemicals across the scoring scale.

The analyses began with equal bin distributions. Both 100 percent of sites with detections and 50 states with releases divide equally into ten bins based on deciles. In the case of Prevalence, the bins provided a fairly good fit to the distribution. However, they still required some adjustment because the equal bins had a tendency to segregate contaminants by type. Contaminants with the highest percent detections scoring a 9 or 10 were ubiquitous inorganics of geologic origin. For example, in the National Inorganic and Radionuclide Survey for ground water, ions such as sodium, calcium, and iron were all detected in ≥ 90% of the groundwater systems sampled. Contaminants with the highest releases were mostly the high-use pesticides applied in nearly all the agricultural states or high-use commodity chemicals with reported discharges from manufacturing or distribution sites in a large number of states such as the Benzene, ethyl benzene, toluene, and xylene impurities in petroleum products.

Creating ten equal bins from the number of states with environmental releases resulted in a scale where a Prevalence score of 10 meant that releases had to be reported from 45 or more States. The workgroup revised the scale for release data so that if more than half the states (25) reported releases the chemical would receive a Prevalence score of 10 and indicate that the contaminants potential for occurrence was relatively high. The percent of detections in finished and ambient water (i.e. percent of systems/sites) were also adjusted to ensure that the most widely detected organic chemicals received more representative scores when compared to the naturally occurring inorganic compounds (IOCs).

Among occurrence data elements, the linkage between the Prevalence measures and Magnitude measures works well for the water measurements and environmental release measures. It does not work well in the cases when only annual Production data are available. The Production data provide a measure of pounds of a chemical product produced annually in the United States but these data do not provide a linked measure such as the number of states in which it is produced or used. This production rate represents the commercial importance of the chemical to some extent. Since high production tonnage suggests wide use of a commodity chemical, the workgroup decided that production data would be used as a measure for likely Prevalence across the country. For example, a chemical produced at a billion pounds per year is more likely to be used and released more widely than a compound produced at only 10,000 pounds per year. Experimentation to examine the correlation of Prevalence scores based on measures of detections in water and the number of states receiving environmental releases, based on production, supported the workgroup hypothesis. Correlations were only fair to good but justified the use of production data as a measure of Prevalence when other data on the spatial spread of a contaminant across the United States are not available.

Following appropriate adjustments to insure that there was adequate representation of organic and inorganic contaminants across the ten point scale and a reasonable distribution of the scores based on release data, the Prevalence scoring scales were finalized. The Prevalence scoring protocol is presented in Appendix A.

2.2.3 Evaluation of the Prevalence Protocol

The relationship between production or even environmental release data and the actual occurrence in drinking water is complex. Exhibit 11 shows the scores for several contaminants based on the finalized Prevalence scoring scales. As expected, in some cases the agreement of

scores across these differing data elements was not good. For example, a chemical like glyphosate scores very high for environmental release (being perhaps the most widely used herbicide in the country) but its water occurrence scores are very low, because of the chemical and physical properties that influence its fate and transport in the environment, restrictions on use locations and drinking water treatment.

Exhibit 11. Comparison of Prevalence Scores for Learning Set Contaminants

Chemical	Potable water samples	Total TRI Releases	Pesticide Applications	Production
	% PWS detect.	# states	# states	lbs/year
Calcium	10	NA	NA	8
Atrazine	9	8	10	7
Glyphosate	2	ND	10	NA
Metribuzin	1	4	10	NA
Toluene	9	10	NA	9
Trichloroethylene	9	10	NA	8
Tetrachloroethane 1,1,2,2	3	6	NA	7

The contaminants in Exhibit 11 indicate that, when the correlation between possible Prevalence scores is weak, the major difference (e.g. glyphosate) is between the finished water score and the production/release scores. This supported the decision to use a hierarchy of data elements for Prevalence. Where actual water measurements are available, they are the Prevalence measure of choice because they are the most direct measures of likely occurrence in drinking water.

The hierarchy selected for use in scoring Prevalence is as follows:

- Percent of PWSs with detections (national scale data)
- Percent of ambient water sites or samples with detections (national scale data)
- Number of states reporting application of the contaminant as a pesticide
- Number of states reporting releases (total) of the chemical
- Production volume in pounds per year

2.2.4 Magnitude - Calibrating Scales and Scoring

To scale the Magnitude attribute, an evaluation to identify possible correlations among data elements was conducted. First, a comprehensive universe of finished water quality data was compiled, including the national occurrence database of regulated contaminants (compiled for the 6-Year Regulatory Review), the historic data from various unregulated contaminant monitoring programs (noted as NCOD Rounds 1 and 2, above), and the data from NIRS. This provided a comprehensive array of data covering the expected distribution range of Magnitude for any new contaminant, ranging from high median concentrations for some naturally occurring inorganic ions or elements to non-detect values for some trace organic chemicals.

The NRC (2001) had initially recommended that Magnitude be scored based on its relationship to Potency. In their pilot study they proposed that the magnitude score be the square root of the median concentration, (based on its position in a decile distribution) times the potency score. A median concentration that fell within the lowest decile of the distribution would receive a 1 and that in the highest decile a 10 for the calculation. The workgroup evaluated the NRC approach to scoring Magnitude and found that it was not feasible for the following reasons:

- The NRC equation cannot be applied when the Magnitude data are based on environmental release or chemical/physical properties.
- A decile distribution for the median concentration values results in low scores for almost all organic chemicals because of the high concentration of geochemical inorganic contaminants present in water (see Exhibit 12)
- Application of the NRC equation did not provide a good measure of relative Magnitude (See aldrin and sodium in Exhibit 12). A high concentration, low Potency combination can receive the same score as a low concentration, high Potency combination.

To examine the efficacy of the NRC approach, the workgroup applied it to six of the chemicals from CCL 1 for which regulatory determinations had been made and, thus, had the necessary Potency and occurrence data. The results of that evaluation are summarized in Exhibit 12.

Exhibit 12. Comparison of the NRC Magnitude Score with the Ratio of the Health Advisory Guideline to the Concentration in Finished Water

Contaminant	Potency Benchmark		Median Concentration		Magnitude	Potency Benchmark: Concentration Ratio
	mg/L	Score	mg/L	Score	NRC score	
Aldrin	0.000002	10	0.0006	1	3.2	0.003
Hexachloro-butadiene	0.0009	7	0.001	1	2.6	0.9
Manganese	0.3	4	0.01	1	2	30
Metribuzin	0.07	5	0.001	1	2.2	70
Naphthalene	0.1	5	0.001	1	2.2	100
Sodium	120	1	16.4	10	3.2	7.3

The Potency Benchmark is the Health Advisory guideline (cancer or non-cancer) for a lifetime exposure for all chemicals except sodium. The guideline for sodium is derived from the recommended dietary intake for sodium in adults, 2.4 g/day÷2L/day using a Relative Source Contribution of 10%
The Potency Scores were derived from the RfD-equivalent or 10^{-6} cancer risk values..
The concentration scores were obtained by using sodium as the upper level for the range and dividing the range into deciles as recommended by NRC.

As indicated in Exhibit 12, the NRC score does not display a consistent relationship to the ratio of the potency-based drinking water guideline to the median finished water concentration. Aldrin, the contaminant from Exhibit 12 that is present in drinking water at the levels of greatest concern has the same magnitude score as sodium ion that is only weakly toxic and not present at a concentration of concern for other than those on very low sodium diets. In addition, as

mentioned above, the decile distribution of concentrations resulted in a score of 1 for any contaminant present in water at concentrations lower than 1.6 mg/L (one tenth of the sodium concentration). Given this distribution, only inorganic contaminants are likely to receive intermediate scores on the concentration scale. Because of the observed limitations in the NRC proposed approach the workgroup determined that it was not appropriate for scoring Magnitude.

The second approach that was investigated employed the use of the Health Reference Level (HRL) to establish the scores for Magnitude. For example, the largest dose that received a Potency score of 10 was converted to an mg/L equivalent using the HRL methodology. Anything less than that concentration received a 1 on the Magnitude scale. Each log-based Potency value was paired with a log-based concentration. A Potency score of 10, when paired with any Magnitude score, would be suggestive of concern because the concentration was greater than the Potency. However a Potency score of 8 would only give rise to concern if the Magnitude score was 3 or greater (see Exhibit 13).

Exhibit 13: Magnitude Concentrations and Scores Derived from Potency Doses

Potency Score	Potency Range mg/kg/day	Concentration equivalent mg/L	Magnitude Score
10	0 to 3.16×10^{-7}	0 to 2.2×10^{-6}	1
9	3.17×10^{-7} to 3.16×10^{-6}	$>2.2 \times 10^{-6}$ to 2.2×10^{-5}	2
8	3.17×10^{-6} to 3.16×10^{-5}	$>2.2 \times 10^{-5}$ to 2.2×10^{-4}	3

This second approach to relating Potency and Magnitude proved to be unwieldy because the two scales are inversely related. It was also problematic because it could not be used for Potency values based on NOAELs, LOAELS, and LD50s, or Magnitudes that were not expressed in concentrations terms. It also did not take into account the differences in the HRL determination process for carcinogens versus non-carcinogens.

The workgroup next explored a variety of potential scales that could be applied to the finished water concentration data without consideration of Potency. The first Exhibits 14A-C illustrate the comparisons of three of the approaches evaluated for the organic and inorganic contaminants. Exhibit 15 shows the differentiation in scores across the three experimental approaches.

The first approach was to develop scales that utilized the array of compiled Magnitude data and 10 bins with approximately equal numbers of contaminants in each bin, referred to as the equal number bins scale in Exhibit 14A. Equal bins did not provide a good dispersion of scores. Accordingly, various log-scale options were explored. The Magnitude data do not range across as many orders of magnitude as the Potency RfD data, so various semi-logarithmic scales were evaluated to better represent the distribution of values across the scale.

In evaluating and developing the calibration scale, the water occurrence data presented a particular challenge because the IOCs tended to skew the results. Many IOCs result from various anthropogenic processes but most are of geologic origin as well, and they have relatively high measures for both Prevalence and Magnitude compared to most organic chemicals. Hence, for some of the semi-logarithmic Magnitude scales (e.g., Half-Log Option A), the only chemicals

that could score high (e.g., a 10 or 9) would be IOCs. Such a scale would depress the score for organic chemicals that are of equally high concern because of their expectedly lower concentrations. One approach that EPA evaluated was using different scales for IOCs and organic chemicals; however, having two scales would make the scoring process complex. To keep the process simple it was decided to use one scale for all water data. Accordingly, the scores were distributed across the range of values so that organic contaminants could receive high scores as well as the IOCs. Comparisons and adjustments were made until the current protocols, using a semi-logarithmic scale (labeled as Half-Log Option B in Exhibit 14C), were selected.

Exhibit 14A. Equal Bins Drinking Water Magnitude Scale

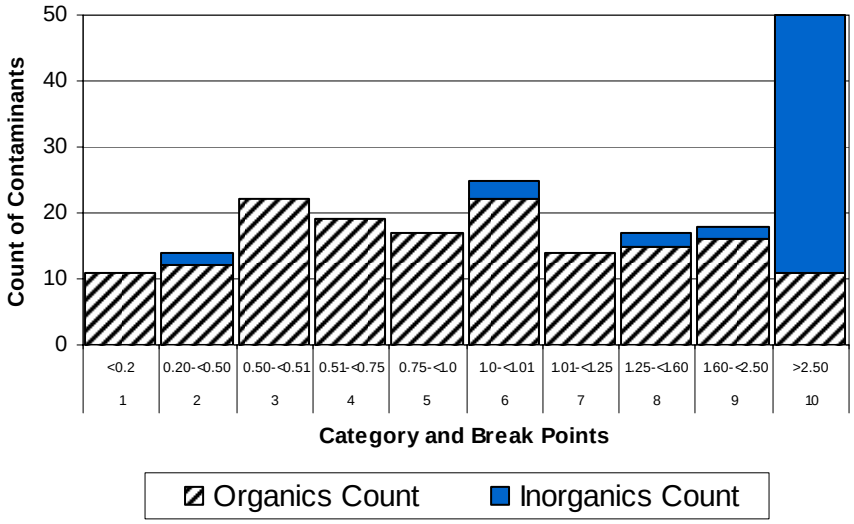


Exhibit 14B. Half Log Option A Drinking Water Magnitude Scale

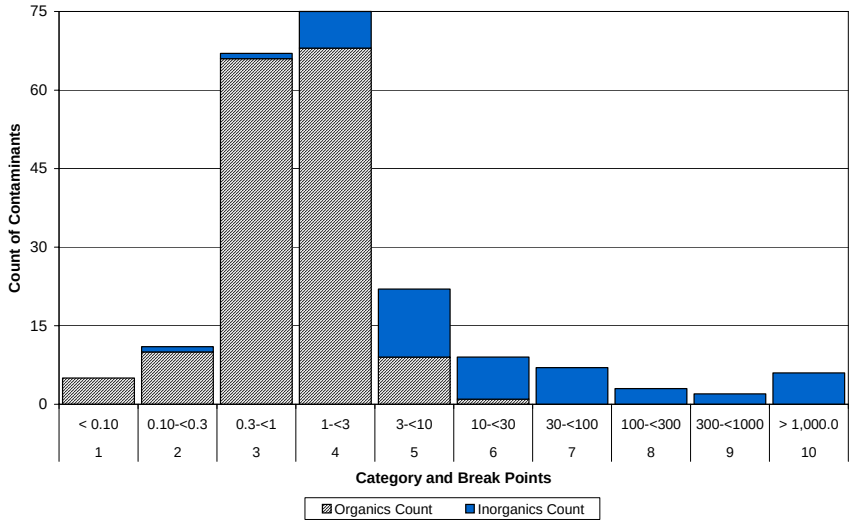


Exhibit 14C. Half Log Option B Drinking Water Magnitude Scale

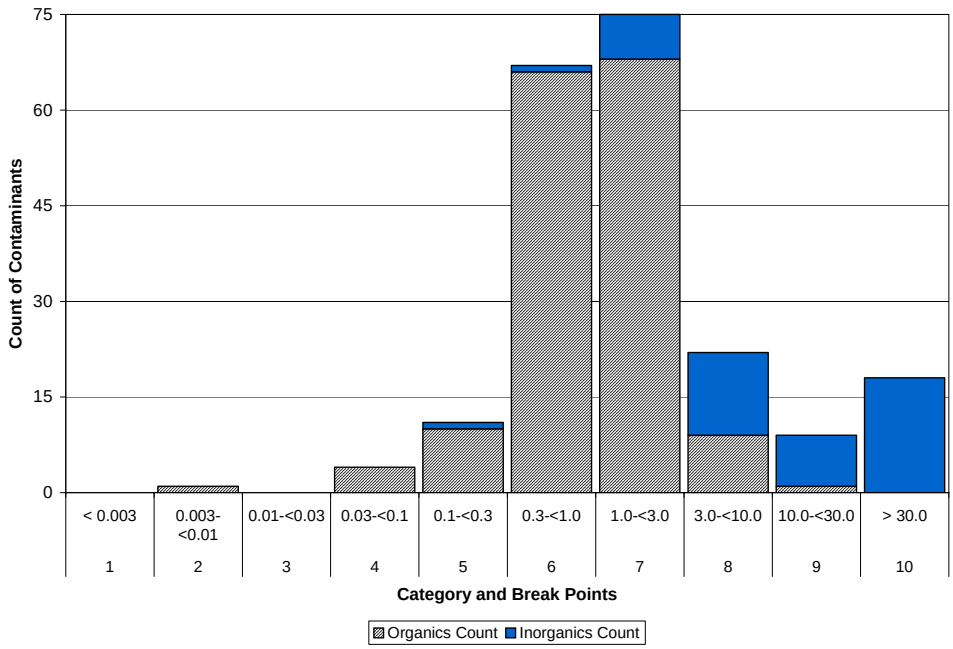


Exhibit 15. Magnitude Attribute Scores: Example Contaminants Scored by their Median of Detections Using the Various Approaches in Exhibit 14.

Chemical	"Bins" *Score*	Half-Log Option A *Score*	Half-Log Option B *Score*
Hexachlorobutadiene	2	2	5
1,1,2,2-Tetrachloroethane	3	3	6
Boron	10	6	10
Sulfate	10	10	10
Antimony	9	4	7
Ethylbenzene	6	4	6
Endothall	10	6	9
Methyl ethyl ketone	5	3	6

When developing the calibration scales for the release data, the ranges of data were similarly arrayed using a scale based on half-log units with a distribution of scores that reflected the distribution of the data in the learning set.

2.2.5 Persistence-Mobility as a Surrogate Measure for Magnitude

In cases where production data are the only measure of occurrence, scoring for Prevalence and Magnitude becomes difficult. The NRC discussed Persistence and Mobility as a fifth attribute and had suggested they could be used to predict possible occurrence if other direct measures were not available. In its review, NDWAC suggested that Persistence and Mobility could provide a surrogate measure of Prevalence with production used as a measure of Magnitude. To examine the NDWAC proposal, the EPA workgroup carried out a series of exercises in which scores for Magnitude derived from concentrations in drinking water and environmental releases were examined to see if they correlated with production scores and with Persistence-Mobility scores calculated using the scoring equation developed by NDWAC. In no case was the correlation as good as one might desire, but it was apparent that the Persistence-Mobility approach showed a better correlation with the Magnitude scores, based on the preferred data elements (concentration/release), than the production information. Accordingly, the workgroup chose to use Persistence-Mobility as a surrogate measure for Magnitude.

Persistence and Mobility are environmental fate parameters. They are considered in combination as a measure of potential occurrence because both transport (i.e. Mobility) and fate (i.e. Persistence) are important when predicting whether a contaminant is likely to be found in water at a specific location, in situations where there is an environmental source for the contaminant. The length of time a chemical remains in the environment before it is degraded (Persistence) affects its importance as a potential drinking water contaminant. Persistence is generally expressed as rate of degradation or half-life ($t_{1/2}$) indicating, in this case, the length of time required for the chemical to degrade to half its original concentration in the medium of interest

(e.g. water). Similarly, the Mobility of a chemical, or its ability to be transported to and in water, affects its potential to reach and dissolve in the source waters for a PWS.

There are a number of data elements that measure the fate of a chemical in the environment. The physical/chemical parameters that are most relevant to the fate in drinking water are summarized in Exhibit 16. The first 4 measures of mobility represent the equilibrium ratio for the partitioning of the contaminant from one medium to another: K_{oc} (sediment: water), K_{ow} (octanol: water), K_d (soil: water) and Henry's Law Coefficient (air: water). K_{oc}, K_{ow} and K_d are sometimes expressed as logs of the original measurements. The measures of persistence each reflect the time the chemical will remain unchanged in the environment.

Exhibit 16. Mobility and Persistence Data Elements

MOBILITY	PERSISTENCE
Organic Carbon Partition Coefficient (K_{oc})	Half-Life
Octanol/Water Partition Coefficient (K_{ow})	Measured Degradation Rate
Soil/Water Distribution Coefficient (K_d)	Modeled Degradation Rate
Henry's Law Coefficient (K_H)	
Solubility	

The data elements listed in the table above are arranged in hierarchical order, with the most desirable at the top (i.e., the first data to be used if available).

Organic Carbon Partitioning Coefficient (K_{oc}) is one of the most common indicators of the mobility of a chemical in water. A high K_{oc} increases the probability that, once a chemical reaches a receiving water body, it will remain bound to sediments or adjacent soils, and thus, slowly partition from the sediment to the water column. A high K_{oc} favors the presence of the contaminant in water for a long time but at low concentrations since the K_{oc} will favor the sediment over the water. A high solubility favors rapid dissolution in the water body from a near-by source and potentially high concentrations if the water source is confined and the environmental release substantial.

2.2.6 Persistence-Mobility Data – Calibrating Scales and Scoring

Many of the measurements of environmental fate properties vary depending on the actual field or laboratory conditions. Some are reported in standard data sources only as ranges, or categorical descriptions. Scoring was further complicated by the fact that two separate environmental fate parameters were used in the scoring of the one attribute. Accordingly, the EPA workgroup selected the approach proposed by NRC and supported by the NDWAC for using the Persistence-Mobility information after experimenting with several other approaches.

The Persistence and Mobility data were arrayed, or partitioned into relatively simple low-medium-high categories as suggested by NRC. Published definitions for the categories were used, such as the categories for K_{oc} from Fetter, 1994 and the classifications for the octanol water partition coefficient (K_{ow}) from Lyman, et al, 1990. The categories are given values of 1, 2, or 3 based on the ranking of the measurement from low to high. The persistence value is averaged

with the mobility value and a multiplier (10/3) is used to translate the score to a 10 point scale (see the Persistence-Mobility Protocol in Appendix A, for details).

Since the persistence and mobility data are being used as a measure of Magnitude, a low ranking (1) for a parameter is one that will minimize the concentration in water and a high ranking (3) is one that will maximize the concentration. For example, a high Koc means that the distribution between the water column and sediment favors the sediment and is ranked a low, while a lower Koc means that the ratio of a contaminant in sediment to that in the water allows a larger portion of the total to be in the water and is ranked as high.

As mentioned above, the workgroup undertook a series of evaluations to compare the Persistence-Mobility scores for selected contaminants to the Magnitude scores derived from the preferred data elements (concentrations in water or environmental releases). Often, data were not available for a half-life or a measured degradation rate for the Persistence value. In these cases, EPA's PBT Profiler was tested and added to the Persistence protocol to ensure both Mobility and Persistence data were used to calculate the attribute score.

The PBT Profiler was developed as a screening tool to identify pollution prevention opportunities for chemicals without experimental data. Among other endpoints, it estimates environmental Persistence for organic chemicals.[7] In addition to estimating a degradation rate, the PBT Profiler also estimates the percentage of a chemical that partitions to soil, sediment, water, and air compartments. As a last option, in cases where other chemical property data are not available, the amount of a chemical that is predicted to partition to the water phase by the PBT Profiler (the percent in water, a measure of solubility) is used to score Mobility.

The workgroup recognized that the Persistence-Mobility protocol can result in relatively high scores (7 to 10) in cases where more direct data elements for scoring are not available. However, given the uncertainty associated with some of the Persistence-Mobility data elements, the workgroup decided the somewhat conservative scores were acceptable as surrogate measures for Magnitude, when only these data were available for scoring.

2.2.7 Evaluation of the Magnitude Protocol

The occurrence data clearly vary in how directly they measure demonstrated or potential occurrence related to drinking water. Exhibit 17 compares the scores for several chemicals using the different measures of Magnitude. In all cases the finished water Magnitude score is higher than the score for ambient water. Scores for pesticide application rates are higher than those for TRI releases. As was the case for Prevalence, the workgroup determined that a hierarchy would be used in scoring Magnitude. The hierarchy developed uses finished water occurrence data if available.

[7] http://www.pbtprofiler.net/ The PBT program will not accept inorganics as input, and identifies the elements, which if present, that prevent the profiling of a particular chemical. The only exceptions to this rule are sodium, potassium, and ammonium salts of organic acids, which can be profiled. Thus, the PBT profiler cannot be used for inorganics or organometallics. However, as drinking water ions, inorganic contaminants are generally present as salts and do not degrade, and thus are assigned a score of "3" – high persistence. See the Appendix A for more complete review.

Exhibit 17. Comparison of Scores derived using the Magnitude Protocol

Chemical	CASRN	Finished Water Concentration	Ambient Water Concentration	Pesticide Release Data	Total TRI	Persistence/ Mobility
		Median (µg/L)	*Median (µg/L)*	*Lbs/year*	*Lbs/year*	
Calcium	7440702	10	--	--	--	10
Atrazine	1912249	6	4	10	8	8
Glyphosate	1071836	2	--	10	--	7
Metribuzin	21087649	7	3	8	2	7
Toluene	108883	6	4	--	7	5
Trichloroethylene	79016	7	4	--	10	10
1,1,2,2 Tetrachloroethane	79345	6	5	--	4	7

The hierarchy suggested for Magnitude draws on the following data sets:

- Median concentration of detections from finished water systems
- Median concentration of detections from ambient water sites or samples
- Amount of pesticide applied
- Amount of total releases
- Persistence-Mobility data

2.3 Fine Tuning the Protocols

As discussed in the previous sections, the workgroup developed and fine-tuned the Attribute Scoring Protocols through a step-wise process of data selection, data analysis, calibration of scales, and evaluation of the functionality of the scores in PCCL to CCL decision-making. The decision-making component of the process examined the ability of the scored attributes to adequately represent the level of concern about contaminants. The testing also evaluated whether or not the scores provide a consistent input to the decision making portion of the CCL listing process that is relatively independent of the type of input data that provides the basis for the score.

Quality assurance measures utilized comparisons of list/ no-list determinations by workgroup experts based on descriptive and quantitative measures of health effects and occurrence (raw data) compared with determinations based on the scored attributes. Differences in decisions were identified. The workgroup discussed those differences and the rationale they had used to reach decisions based on the raw data versus the scored data. Minor adjustments were made to the scoring protocols based on those discussions.

Using a training data set of contaminants (Chapter 3), blinded test-case decisions made with raw data versus scored results, or decisions based on one data element in a hierarchy versus another, were compared. The results provided a high level of confidence that the scores, while not capturing all information experts used in making decisions based on raw data, adequately captured the critical relationships that informed the EPA workgroup "list" versus "don't list" determinations.

3.0 DEFINITIONS AND OVERVIEW OF THE TRAINING DATA SET

This chapter describes the process used to identify a set of chemicals to train (or calibrate) the classification models discussed in the next chapter. The raw data, attribute scores, and protocols discussed in chapter 2 were applied to these contaminants and that information is carried forward in the evaluation of classification models discussed in Chapter 4.

The training data set (TDS) for chemicals is the set of data used to train (or teach) the classification models to mimic expert list-not list decisions. The TDS used to train the models for CCL 3 was comprised of 202 discrete sets of attribute scores for contaminants and consensus list-not list decisions made by a team of EPA subject matter experts.

Classification models are algorithms that use statistical approaches for pattern recognition and derive mathematical relationships among input variables (measurements or descriptive data) and output from a TDS. For the CCL, the classification models are used to develop a relationship between the contaminant attribute scores (input variables) and the classification of these contaminants into list-not list categories (output). The mathematical relationship between attribute scores and list-not list decisions is determined based on the classification decisions on TDS chemicals and their associated data. Once the TDS is used to train the classification model, the model is then applied to a larger list of contaminants to predict their likely list-not list classifications.

The process for developing the TDS utilized EPA subject matter experts familiar with the technical aspects of the attribute data and the selection of drinking water contaminants for listing and regulation.

3.1 Key Considerations

EPA considered the following key factors in developing the training data set:

- Selection of contaminants representing a range of outcomes and decisions likely to be encountered in developing a CCL;
- A variety of input data ensuring adequate coverage of attribute scores and combinations of scores;
- Chemicals that, when present in drinking water, would present a meaningful opportunity for public health improvement if regulated; and
- Contaminants that would likely be selected for the PCCL.

3.2 Developing Key Components of the Training Data Set

3.2.1 Attribute Scores

Attribute scores are a critical component of the TDS, as mentioned in Chapter 2. The TDS used for training the classification models consisted of attribute scores for 202 contaminants. A set of known chemicals was chosen to develop the TDS and supplemented with a range of attribute scores that represented hypothetical or artificial contaminants. These artificial contaminants were developed to fill voids in the space of possible attribute scores and improve classification model results.

3.2.1.1 Attribute scores for real contaminants

Initially, EPA selected "data rich" contaminants from among regulated contaminants and previous CCLs because they had a range of readily available occurrence and health effects information. EPA drinking water subject matter experts and stakeholders (as part of the NDWAC process) reviewed the initial list of contaminants and identified candidates for the TDS. Based upon an NRC and NDWAC recommendation, EPA also added chemicals "generally regarded as safe" by the U.S. Food and Drug Administration to provide adequate coverage of possible attribute inputs and a range of list-not list decisions. This initial selection process identified 51 chemical contaminants for the TDS.

Subsequently, EPA chose 50 additional contaminants from the CCL 3 Universe. These 50 contaminants were randomly selected from those with high health effects toxicity levels that had occurrence data because they represented contaminants likely to make it to the PCCL. The addition of these 50 contaminants resulted in 101 contaminants with data to score attributes.

To aid in the review and evaluation, data summary sheets were prepared for each contaminant that included a range of available health effects, occurrence, and environmental fate data. All the available health effects and occurrence, use, and fate data that could be used to develop the attribute scores for Potency, Severity, Magnitude and Prevalence were included on the individual summary sheets. Samples of the data summary sheets are presented in Appendix B.

While contaminant names were included in the initial evaluations, expert reviewers found that knowledge of the contaminant name introduced bias into the decision-making process. Subsequently, EPA "blinded" contaminant names or identifiers in contaminant evaluations to increase objectivity and force decisions to be made solely on the available data and associated attribute scores. The names of contaminants were revealed after the "blinded" evaluations. The attribute scores were developed according to the Attribute Scoring Protocols discussed in Chapter 2 and presented in Appendix A.

3.2.1.2 Attribute scores for hypothetical contaminants

The performance of the classification models using the initial TDS gave an indication of gaps in the possible attribute space that the set of 101 TDS contaminants did not adequately cover. This led EPA to add a set of 101 hypothetical contaminants to the TDS. These contaminants had specific combinations of attribute scores designed to fill gaps in the space defined by all possible attribute scores and to improve the performance of the models. The majority of these possible scores were selected using Latin hypercube sampling from the set of all possible attribute score combinations, as seen in Exhibit 18 (NIST, 2006). Five contaminants were selected at random from each of the 16 "cubes" represented by the combinations of high (6-10) and low (1-5) scores for the four attributes. This selection resulted in 80 hypothetical contaminants. Twenty one additional contaminants were deliberately selected to fill in some obvious voids in the 4-attribute space, resulting in 101 artificial contaminants.

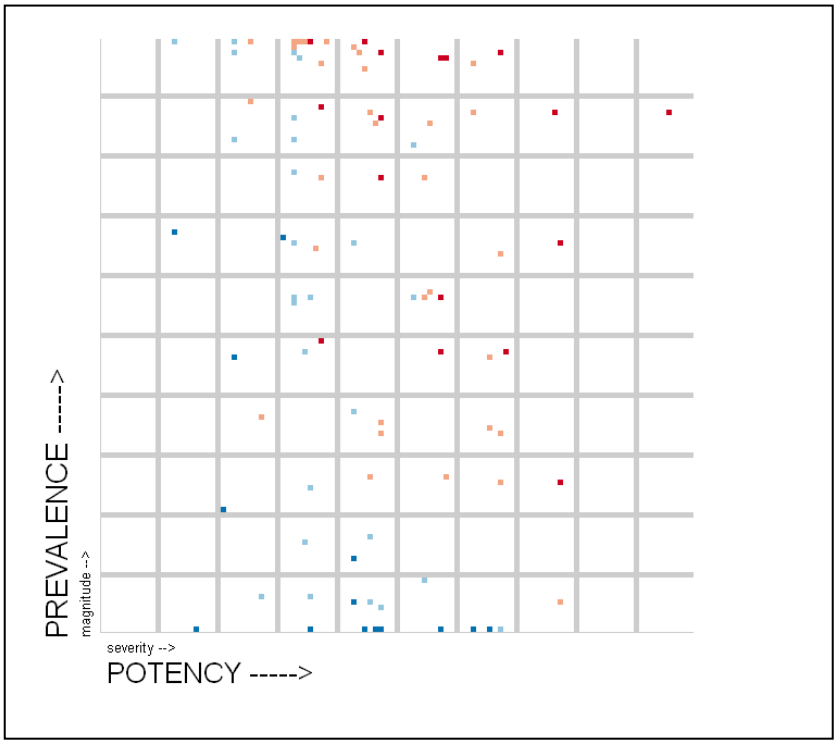
Exhibit 18. Combinations of low and high attribute scores[1] for the four attributes using Latin Hypercube Sampling.

Potency	Severity	Prevalence	Magnitude
Low	Low	Low	Low
Low	Low	Low	High
Low	Low	High	Low
Low	Low	High	High
Low	High	Low	Low
Low	High	Low	High
Low	High	High	Low
Low	High	High	High
High	Low	Low	Low
High	Low	Low	High
High	Low	High	Low
High	Low	High	High
High	High	Low	Low
High	High	Low	High
High	High	High	Low
High	High	High	High

[1] Low scores are randomly sampled from the range 1-5.
[1] High scores are randomly sampled from the range 6-10.

Exhibit 19 displays the attribute space coverage of the 101 contaminants compared to the attribute space coverage of the TDS of 202 contaminants. The combination of real and artificial contaminants resulted in 202 scored candidates that became the TDS. The total attribute space for a model that includes four attributes with scores from 1 to 10 is 10,000 combinations of possible attribute scores. Each point plotted in Exhibit 19 represents one chemical in the TDS and one of the 10,000 possible combinations of attribute scores.

Exhibit 19. Attribute Space for the 101 TDS compared to that for the 202 TDS



This graphical analysis shows five elements of the model results, the four attributes evaluated and the categorical decision (L, L?, NL?, and NL) in a single graph. Note in Exhibit 19 that the vertical and horizontal axes show two attributes on each axis. The attribute scores for Potency are the large squares across the horizontal axis. The corresponding score for Severity is a separate scale within each larger square. That is, each Potency square has a range of Severity scores. Similarly the Prevalence and Magnitude scores are plotted on the vertical axis, Prevalence as the large squares along the vertical axis and Magnitude as a separate square within each larger square. The decision category assigned each potential attribute is color coded (NL decisions are denoted by dark blue, NL? by lighter blue, L? by peach, and L decisions by red).

3.2.2 Making List-Not list Decisions

List-not list decisions are the second key component of the TDS, as mentioned in Chapter 3. The EPA subject matter experts made list-not list decisions on an individual basis and as a group, based on attribute scores and based on data that had not been converted to attribute scores (actual or raw data). The development of the list-not list decisions was an iterative process that incorporated revisions to the attribute scoring protocols, and the final list-not list decisions, as experience was gained by the EPA experts. Differences between the decisions based on the scored attributes and the raw data were resolved by revising the scoring protocols to improve the correlation of scores to the raw data.

After evaluating the health effects and occurrence data for each contaminant, each individual reviewer made decisions about how to classify the contaminant, and then met as a group to discuss their decisions. Early in the process the reviewers recognized that clear List or No-List decisions could easily be made for some contaminants, but not for other contaminants. The chemicals in the later group were placed into categories of List? (L?) or Not list? (NL?), in which L? signifies that the decision is leaning towards listing but with some uncertainty, and NL? signifies that the decision is leaning towards not listing, but with some uncertainty. These additional two categories were incorporated into the evaluation process.

As part of the iterative process, the reviewers discussed their classification results and made adjustments to the process, accordingly. When adjustments changed attribute scoring protocols, TDS contaminants were rescored and reevaluated. Individual decisions were made separately based upon either the raw data or attribute scores. Decisions based upon raw data utilized health effects and occurrence data elements, as well as supporting information on fate and uses. For decisions based on attribute scores, only the numeric individual scores were used. The scores were developed from the raw data using the protocols, for Potency, Severity, Prevalence, and Magnitude. In both cases, this evaluation was conducted "blinded," meaning contaminant names were not shown. Appendix C shows an example of summary decisions based upon raw data and attribute scores. For each contaminant, comparisons were made between the list – not list decisions based upon raw data and those based on scores. Reviewers discussed the similarities and differences on an individual contaminant basis, and revised the attribute protocols to reflect decisions made on the actual data (see Chapter 2).

Once L/NL classification decisions were made based on the attribute scores using the revised protocols, consensus among the EPA subject matter experts was used as the final decision for each contaminant. This consensus decision was used to train the models and is further discussed in Chapter 4. Consensus decisions were made by averaging the numerical decisions of

individual reviewers (L = 4, L? = 3, NL? = 2, and NL=1) and rounding to the nearest integer. The rounded averages became the consensus values used to train and evaluate the models (Chapter 4). Appendix C also provides the consensus decisions for each TDS contaminant.

4.0 PROTOTYPE CLASSIFICATION MODELS AND THE CCL PROCESS

The NRC recommended EPA use prototype classification models for CCL selection, citing the limitations of expert processes and other rule-based models. NDWAC agreed that EPA should use a prototype model, also noting that this should improve the reproducibility and transparency in the process. This kind of approach does not eliminate subjectivity but rather, makes the judgments more explicit.

Prototype classification models are often described as pattern recognition models. These models develop statistical relationships (to recognize the patterns) among input variables (attributes, discussed in Chapter 2) of drinking water contaminants to predict their classification ("List," "List?," "Not List?," and "Not List"). The model determines the relationship or rule that links the input to the output based on the decisions made on the TDS (Chapter 3) and then uses that relationship to classify PCCL contaminants based on their attribute scores.

In its study, the NRC experimented with a linear discriminant model and with an artificial neural network (ANN) model to demonstrate the use of classification approaches. EPA, working with NDWAC, identified the following classes of models for evaluation:

- Artificial Neural Networks,
- Classification Decision Trees (with univariate and multivariate splitting rules)
- Linear Models, and
- Multivariate Adaptive Regression Splines (MARS)

The model evaluation was a two-step process. First was the evaluation and selection of the most appropriate ("best-fit") model from within each of the model classes. The second step was the evaluation of the performance of the best models selected from each class. Following these evaluations, two classes of models were rejected and three were maintained to inform the final expert review process.

Artificial Neural Networks (ANNs) - ANNs are information processing models conceptually based on the human nervous system and its learning processes. ANNs apply flexible and often very complex parameterization. Their value is that they use flexible, non-linear functions that can capture almost any kind of underlying relationship between input and output data. For classification purposes, ANNs apply weighting in non-linear functions and do not specify a strict functional form (such as quadratic or cubic equations) as do many statistical models.

Classification Decision Trees - The decision tree classifies the sample by devising a series of tests (or rules, from the TDS) that are mutually exclusive in outcome. The graphical tree is derived with a test at a node in the tree with outcomes from the test branching from each node. Hence, in moving through the tree a contaminant encounters the test at a node, and is sent down one branch or another based on how its attribute meets the test criterion, usually a simple inequality, such as is Magnitude < 3.5 (true or false). Eventually the contaminant reaches a

terminal node (the last node, that no longer branches) that assigns the classification (e.g., category 2 = NL?). Two types of decision tree models were explored, Classification and Regression Tree (CART) which utilized univariate (one attribute at a time) tests at nodes, and the Quick, Unbiased, Efficient Statistical Tree (QUEST) model, which utilized multivariate (weighted sum of all attributes) tests at all nodes of the tree.

Linear Models – General Linear Models - Two types of linear models were tried. A Logistic regression model was applied to deal with CCL's categorical data. The Logistic model was only attempted using two categories (List and Not List). EPA found that the binary approach was not satisfactory, and moved to a four category approach. Recognizing that the ANN models often employ logistic regression, to avoid duplication, the Logistic model was dropped from the final evaluations. Consequently, the data were adapted for use with a regular Linear regression model. This model estimates the workgroup's average classification (on a scale of 1 to 4; 1 = Not List, 2 = Not List?, etc.) for each contaminant as a linear combination of the contaminant's four attribute scores.

Multivariate Adaptive Regression Splines (MARS) - MARS is a non-parametric classification model sometimes referred to as a statistical neural network model. MARS has become widely used in data mining and exploratory analysis because it doesn't assume or impose any particular class of relationship (such as linear or logistic) on all the predictor variables and the outcomes. It can develop different regression relationships for different input variables.

4.1 Model Training and Development

Some software packages are designed to build, fit, and test models internally, while others require an expert user to develop the model. Generally, models are evaluated based on:

- the number of attributes that the model is able to consider,
- the types of relationships or mathematical functions that the model utilizes, and
- the model's ability to predict classification of the TDS.

For example, training a model can involve estimating the values of rule coefficients (such as β_0 and β_1 in the simple linear regression model $Y = \beta_0 + \beta_1 X + \varepsilon$), or determining some other aspect of model structure (such as the number of splits in a regression tree model) to improve how well the model classifies the existing data. Ideally, this training process minimizes the model's predictive error, thereby reducing incorrect model predictions.

"Over-fitting" is a concern when selecting a model. Any of the model classes can be made to fit a particular data set very well by making the model more complex (this usually means estimating more model parameters). However, the addition of model complexity can come at the cost of a loss of general applicability; the added complexity may capture the idiosyncrasies of the specific data set, but may not be representative of the broader processes that generate the data, and hence, may not perform well when applied to an unknown sample. Several methods were used as guidance to avoid over-fitting, depending on the specific type of model being tested.

Software designed specifically for CART, ANN, and MARS were used for those methods. Appendix D lists the specific software sources that were used. These programs provide the user with a number of options to control the model building process. For example, QUEST software,

used to produce a classification decision tree model with linear discriminant nodes, allows the user to specify the following:

- Minimal node size of the tree
- Splitting method (linear or univariate discriminants)
- Splitting criterion (likelihood ration, Pearson chi-square, etc.)
- Pruning method (by coefficient of variation or by test sample)
- Number of fold for cross-validation

After the user selects the control options, the software does its best to fit the training data set. In general, the user is not able to view precisely how the software does its job, but is shown the final model, some statistics regarding its performance, and an indication of other alternatives that were considered. For example, the QUEST software outputs a list of decision trees and their summary statistics (numbers of nodes, error rates). QUEST also identifies the optimal tree and provides the tree's decision rule. In addition, QUEST reports the results of cross-validation tests, in which subsets of the training data are held back. The algorithm produces a rule to best fit the remaining data and this rule is then applied to the data that were held back. This gives a slightly greater error rate because (a) fewer data are used to estimate the model parameters and (b) data used for checking are independent of those used to estimate the parameters. Exhibits 20a and 20b compare QUEST Classifications based on the full training data set (Exhibit 20a) and 5-fold cross-validation (Exhibit 20b).

Exhibit 20a. QUEST Classifications Based on the Full Training Data Set

(shaded cells are exact match with Expert Decisions)

Consensus Blinded Decisions	**Model Decisions**			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	42	0	0	0
3 (L?)	13	41	2	0
2 (NL?)	0	8	54	3
1 (NL)	0	0	2	37

Exhibit 20b. QUEST Classifications Based on 5-Fold Cross-Validation

(shaded cells are exact match with Expert Decisions)

Consensus Blinded Decisions	**Model Decisions**			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	41	1	0	0
3 (L?)	14	37	5	0
2 (NL?)	0	10	50	5
1 (NL)	0	0	8	31

Unlike other models, the simple linear model did not depend on special software. Under this model, the average classification of the experts for a contaminant was estimated as a linear combination of attribute scores. Letting Y[i] be the expert's average classification for training set contaminant i, the model equation is:

$$Y[i] = b_0 + b_{Pot} * Pot[i] + b_{Sev} * Sev[i] + b_{Prev} * Prev[i] + b_{Mag} * Mag[i] + \varepsilon$$

An intercept term (b_0) and coefficients for the four attributes (b_{Pot}, b_{Sev}, b_{Prev}, and b_{Mag}) were selected to maximize the likelihood of the TDS average classifications, given normal error structure (ε is an error term that is normally distributed with mean zero). A residuals plot revealed that unanimous List and unanimous Not List contaminants were often predicted to have extreme errors, suggesting that perhaps the subject matter experts would have assigned some of these to more extreme categories, had they been available. Without censoring, the unanimous Lists were treated as observations of exactly 4.0 and the unanimous Not Lists were treated as observations of exactly 1.0. Recognizing that these may be censored values, they are treated as $\geq$ 4.0 and $\leq$ 1.0, and the likelihood function is adjusted to include these as probability masses (probability of at least 4.0 and probability of at most 1.0) rather than probability densities (probability of exactly 4.0 and exactly 1.0). Maximum likelihood parameters appear to fit the data very well, and predict most TDS average decisions to within 0.25 units.

4.2 Model Sensitivity Analyses

Some analyses that were performed in the development process may be considered sensitivity analyses. These included the following:

- Training the models on subsets of the TDS. This included the partial TDS (as it was being developed) and cross-validation exercises, wherein randomly-selected contaminants were held back from training to provide independent error checks.
- Training after selected "outliers" are removed from the TDS. Those found to have strong influence on the overall performance were investigated further to see if there were valid reasons for excluding them from the TDS.
- Graphical and statistical analyses to identify significant differences in attribute "weights" or influence on model performance. If any attribute had been found to be insignificant, it could have been ignored, perhaps saving some data development resources. (Though attributes were found to have different weights, none was found to be insignificant.)

Rather than detail all of the sensitivity analyses conducted for all classes of models, the remainder of this chapter illustrates the analyses described above using selected applications.

4.2.1 Training with subsets of the TDS

Cross validation for QUEST is described under 4.1, above. Training with early subsets of the TDS (50 and 102 contaminants) produced mixed results for the five model classes. QUEST and linear models exhibited no logical inconsistencies, but ANN, MARS, and CART showed some serious problems. Most dramatic was MARS, which placed contaminants with the very lowest health effects and occurrence scores in the List category. Clearly, additional training data was needed to overcome these difficulties. No class of model was eliminated on the basis of these findings.

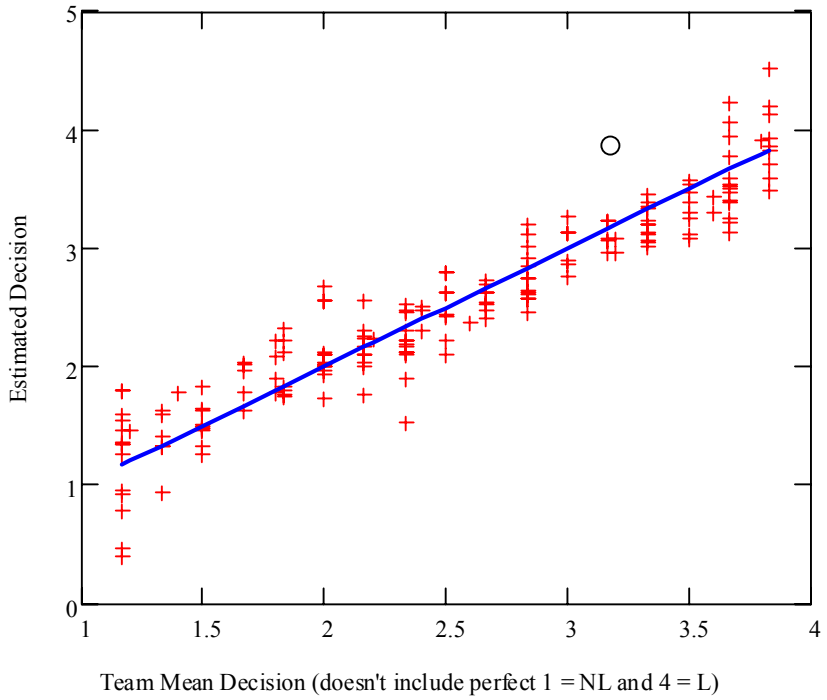
The final TDS (size 202) allowed all of the classes to improve their performance. ANN was found to have no logical inconsistencies. Although MARS and CART improved significantly, both had some areas of non-monotonicity. This means that there were some cases an increasing attribute score could lead to a decreasing classification for a contaminant. (This inconsistency is discussed and displayed graphically in Section 4.4.2.)

4.2.2 Training after Selected "Outliers" Are Removed From the TDS

The linear model was most sensitive to selected TDS contaminants. Fortunately, this model provided a number of tools for identifying outliers. While other models had the objective of minimizing the count of classification errors (or in the case of QUEST, a weighted sum of classification errors), the linear model attempted to minimize the deviance between its prediction and the average classifications for TDS contaminants. When the other models encountered an outlier, (for example, a contaminant with very high attribute scores, but a classification of NL), they did not attempt to make the correct classification for the outlier because that would have meant making other errors for nearby contaminants. Including or not including such an outlier had no effect on the outcome. The linear model, in essence, attempted to minimize the squared estimation error, so outliers tended to have some influence on the linear model parameters.

Residuals plots such as Exhibit 21 revealed potentially important outliers for the linear model. Exhibit 21 shows the model-estimated versus team classification of one important outlier: a contaminant with scores (4, 8, 10, and 10) with a team-average classification of 3.17 (L?) and model-estimated value of 3.88 (L). Another contaminant has as large a residual (model = 1.53 and team = 2.33, both NL?). However, when the model was run first with one and then the other contaminant removed, only the first outlier was found to have a marked influence on the overall error rate (number of misclassifications and weighted sum of misclassifications). When EPA's team was asked about these two contaminants, they agreed that their classification for the first contaminant was influenced by their belief that it was a ubiquitous inorganic that should probably not be listed. When asked how the model should treat PCCL contaminants with such high Severity and occurrence levels, the team agreed that the correct decision would probably be to List the contaminant, but that the two tens for occurrence suggested that the contaminant was inorganic biasing them towards the lower decision category. It was decided to drop this contaminant from training the linear model. Because it had negligible influence on the other models, it was included for them.

Exhibit 21. Model-estimated versus Team Average Classification for the TDS



The graphical displays discussed in Section 4.3.2 were used as additional checks for outliers. The outliers for the linear model were apparent when the training data set was plotted against the background display. The inorganic contaminant that was eliminated from linear model training was seen to fall "between" two other contaminants that were both assigned to the List category – further evidence that its classification of L? may have been inappropriate, at least for the purpose of training this model.

4.2.3 Graphical and Statistical Analyses to Identify Significant Differences in Attribute "Weights" Or Influence on Model Performance

Graphical displays of model outputs (Section 4.3.2) revealed that all of the attributes were important. The ANN graph is the only means of studying the ANN rule, but QUEST and the linear model provide mathematical expressions that clarify the roles of the four attributes. For QUEST, each "node" of the tree involves comparing a weighted sum of attribute scores with a threshold. If the threshold is surpassed, then the "right" path is taken, otherwise, the "left" path is taken. The QUEST software is capable of using fewer than four attributes, and when trained with about half of the 202 TDS contaminants, it sometimes used only three of the four. When the full TDS was used, however, all four attributes were used at each of the final tree's seven nodes. At each node, the four attributes can be ranked in order of their model coefficient. Exhibit 22 shows the ranking of attributes for the nodes of the final QUEST tree.

Exhibit 22. Relative Weights of Attributes at QUEST Nodes

(1 = greatest weight, 4 = least weight)

Node # [1]	Pot	Sev	Prev	Mag	N [2]
1	1	2	4	3	202
2	1	2	4	3	141
3	2	1	3	4	61
4	1	3	4	2	52
5	1	2	4	3	89
7	1	3	4	2	18
28	2	1	3	4	23

[1] Numbers as assigned by QUEST.

[2] N = Number of TDS contaminants that are evaluated at the node. All 202 are evaluated at the first node. Of these, 141 proceed to node 2, while the remaining 61 pass to node 3.

Overall, it appears the Potency carries the most weight, followed by Severity, Prevalence, and Magnitude.

The linear model assigns a weight to each attribute and the greatest of these is that of Potency, followed by Severity, Magnitude, and Prevalence. The order of Prevalence and Magnitude is the reverse of that found for QUEST. The linear model also provides a means of testing the statistical significance of the intercept and four coefficients. Because the model accounts for possible censoring, this testing is not as simple as in a least-squares regression. Two methods were used to approximate the covariance matrix for this model. The first is based on the Fisher information (J(model parameters θ)), derived using the likelihood function, L(data|θ):

$$\mathbf{J(\theta) = - E\,[d^2\,ln(L(data|\theta))\,/\,d\theta^2\,|\,\theta]}$$

The second used a Bayesian posterior sample of parameter values. This sample produced a covariance matrix that was nearly identical to that derived from the Fisher information, suggesting that the likelihood and posterior are very nearly multivariate normal. Hypothesis tests could therefore be conducted using the Markov Chain Monte Carlo (MCMC) sample (10,000 sets of parameter values). Exhibit 23 below shows means, medians, and 95% credible intervals for the model parameters. b1 through b4 are the parameters for the four attributes (Potency, Severity, Prevalence, and Magnitude, respectively), b0 is an intercept term, and Phi is the precision (inverse of the error variance). The 95% intervals reveal that all of the attribute parameters are statistically significantly greater than zero.

Exhibit 23. Summary Statistics from MCMC Sample

Parameter	Mean	2.5%	Median	97.5%
b0	-1.674	-1.865	-1.673	-1.488
b1	0.2410	0.3343	0.241	0.2591
b2	0.2170	0.2002	0.2169	0.2342
b3	0.1157	0.1033	0.1157	0.1284
b4	0.1699	0.1539	0.1699	0.1858
Phi	14.25	11.44	14.22	17.41

Based on the MCMC sample, pair wise comparisons of attribute parameters were all found to be statistically significant. Separate weights are needed for the two health effects attributes and for the two occurrence attributes.

4.3 Model Performance Testing

The TDS, Attribute Scoring Protocols, and prototype model test results were linked together in an iterative process. Testing of the models in the early stages was impacted by changes and refinements in attribute scales, resulting changes in the scores, and changes in the composition of the TDS. These changes required iterative reevaluation of the models and resulted in many improvements that are part of this final analysis. Refinements in scoring are discussed further in Chapter 2 and development of the TDS in Chapter 3. EPA also evaluated the impact of the attributes used by the models and the effects of missing data on the performance of the models during the various stages of development.

During early stages of the model testing, the models were run with various sized TDSs. The CART and MARS models did not always use all four attributes with some of the smaller TDSs. However, all models used all four attributes when trained with the final TDS, consisting of 202 contaminants.

Exploratory analysis of the results revealed some additional problems with the CART and MARS models. When two contaminants have identical attribute scores for all but one attribute, the contaminant with the higher score for that attribute should logically be classified at least as high as the contaminant with the lower score. For example, if a contaminant with scores (4, 4, 4, 4) is assigned to the L? Category, then a contaminant with scores (4, 4, 4, 5) should not be assigned lower, to category NL? or NL. Both CART and MARS rules had this type of misclassification. Both models did not consistently classify contaminants. Another problem with the CART and MARS models was their errors across two categories. Both models did not consistently separate the NL? from the L contaminants or separate the L? from the NL contaminants. Because of these problems, and because of poor performance with respect to the training set decisions, these two models were not selected to inform PCCL to CCL EPA decisions.

Three models, ANN, QUEST and Linear regression consistently demonstrated the best performance when using the TDS. Exhibit 24 lists the features of these three models.

Exhibit 24. Features of the Three Preferred Models Based on TDS Test Results

Features	Classification Models		
	Artificial Neural Network	**Classification Tree with Linear Nodes (QUEST)**	**Linear Regression**
Objective Function (to be minimized or maximized)	Minimize count of training set errors	Minimize count of training set error loss OR minimize error loss	Maximize likelihood or minimize error loss
Prediction	Rounded average workgroup classification	Rounded average workgroup classification	Average workgroup classification (not rounded)
Ranking Capability	Rank by Probability (Pr of List)	Rank by classification and distance from discriminant (requires post-processing)	Rank by prediction
Transparency of Optimization Method	Not transparent	Not transparent	Simple and transparent
Classification Rule	Not clear, but classifications available for all attribute score combinations.	Clear. Complex classification tree with linear inequalities for intermediate nodes	Clear. Simple linear function of attribute scores.
Computation Speed	< 1 Second	< 1 Second (but process for deriving distances for ranking is not part of software)	< 1 Second
Software Cost	Version used is Freeware.	Freeware	No special software

4.4 Evaluating Classification Differences

This section describes how the classification models were assessed and compared with respect to:

- The number of correct and incorrect classifications for the 202 TDS contaminants
- The number of "large" misclassifications (off by more than one category)
- The weighted sum of TDS classification errors
- Ability to identify intermediate classifications
- Consistent behavior (e.g., no decreasing classification as attribute scores increase)

As described in Section 3.3.1, the approach to classifying the TDS contaminants became a four-category decision (L, L?, NL?, and NL) to allow the EPA subject experts, experienced in making L/NL decisions, to identify the decisions that were not strong list or NL decisions. Accordingly, quantification of model performance as it compared with the decisions of the EPA subject matter experts had to consider a suite of various misclassification outcomes, (Exhibit 21) such as a consensus decision that a contaminant should be a L?, but the model classifying it as a L. However, not all the misclassifications are considered to be equally serious. Of the differences, the most substantive would be placing a strong "List" contaminant in the "Not List" category. This might result in missing a key candidate for the CCL. Considering the relative seriousness of the different kinds of misclassifications, the workgroup represented the classification error losses in terms of the weights displayed in Exhibit 25. Initially, the table had equal weights for all misclassifications and these were adjusted until the workgroup was comfortable that they represented the relative significance of the 12 misclassifications or errors that are possible. The most serious error (placing a List contaminant in the Not List category) has ten times the weight (i.e., a 10) of the least substantive difference (placing a contaminant one category too high, such as placing a List? contaminant in the List category, i.e., a value of 1).

Exhibit 25. Decision Comparison Matrix; Weight of Differences

Model Decisions	Subject Matter Expert Decisions			
	Not list	**Not list?**	**List?**	**List**
Not list		2	5	**10**
Not list?	**1**		2	5
List?	2	**1**		2
List	3	2	**1**	

The Decision Comparison Matrix and the quantitative weighting of differences were used to compare model results to EPA decisions. This was part of the process to minimize the losses and cost of the misclassifications.

The models are tools to help classify and prioritize the contaminants for expert review at the end of the CCL process. After applying the models, EPA plans to scrutinize all of the contaminants identified as "List," but likely will spend less evaluation time on those placed in the other categories (particularly the "Not List"). As a result, the EPA workgroup recognized the need to minimize the likelihood of classifying "List" contaminants as "Not List" or "Not List?" and applied the Decisions Comparison Matrix as a tool in evaluating model output misclassifications.

4.4.1 Classification Differences Among the Models

Appendix E describes the classification rules or "solutions" that were generated by the different models. These rules perform differently, when compared with the TDS consensus decisions. Exhibit 26 summarizes the number of each type of decision by each model compared to the subject matter expert consensus decisions and Exhibit 27 summarizes the results and the

Weighted Loss Value. The model input (and output) for ANN, CART, MARS, and QUEST were the integers representing the classes (i.e., 4=L, through 1=NL) while the Linear model estimated the average classification. When a majority of decision makers favored one classification for a contaminant, that class was assigned. When the decision makers were evenly split (for example, if three assigned a contaminant to 1 (NL) and three assigned it to 2 (NL?)), an agreement was reached to assign the contaminant to the higher of the two categories (2 (NL?) in the case of even split between 1 and 2). In contrast, the Linear model predicted the average classification and was trained using average classifications for the TDS. For example, if three decision makers assigned a contaminant to 1 and three assigned it to 2, the average classification was 1.5.

Exhibit 26. Summary of Quaternary Model Decisions

Decision Category	Number of Decisions in Category by Model					
	Expert Workgroup Blinded Decision	ANN	CART	Linear	MARS	QUEST
4 (L)	42	42	27	27	47	55
3 (L?)	56	55	68	69	38	49
2 (NL?)	65	65	73	69	81	58
1 (NL)	39	40	34	37	36	40
Total	202	202	202	202	202	202

Exhibit 27. Results of 202 Model Classifications and Weighted Misclassifications

	Number of Classification matching TDS	Weighted Loss Value
ANN	168	52
CART	156	84
Linear	160	72
MARS	160	67
QUEST	174	33

While there are important differences, all the models were able to process the TDS and produce classification rules. All five models produced from 79% to 86% exact matches with the consensus decisions. Exhibit 28 provides further details on the predicted classifications for each model. Perhaps most important, no model classed any consensus L(4) or L?(3) decision as a NL (1). Only CART classed any L(4) candidates (2%) as NL?(2).

The best performance, by these metrics, was that from the QUEST model, while the lowest performance was by CART. The objective of the QUEST model was to minimize the value loss of the misclassifications, while the other methods minimized errors with no regard for the

weights shown in Exhibit 25. As a result, QUEST has the lowest loss, and the highest exact match rate. Note on Exhibit 28, that QUEST's misclassifications are all shifted to the "left;" i.e., QUEST only predicted 2 of consensus L? decisions would be NL?; and 8 of consensus NL? were predicted to be L?, a more acceptable and conservative difference. ANN attempts to maximize the likelihood of correct predictions and simply minimize the number of misclassifications (not their weighted value). Its misclassifications are rather equally distributed around the exact match categories. The performance of MARS and the Linear model look similar, but MARS had the highest value of any model for consensus L? decisions that were predicted as NL? (16).

4.4.2 Logical Evaluation of the Models – Graphical Analysis

As introduced in Section 3.2.1, the testing of the models included evaluation of the total potential "attribute space." The total "attribute space" for a model that includes four attributes with scores from 1 to 10, is 10,000 combinations of possible attribute scores. The graphical analysis of model performance looked at how the models generated decisions on the category to which it assigned contaminants (L or NL). When applied across the entire attribute space, the discriminate surfaces that bound the model's decisions on the category to which it assigned any possible score became apparent. These category boundaries or discriminant surfaces were reviewed for consistency through the graphical analysis. Five models (ANN, QUEST, MARS, CART, and Linear Regression) developed with the 202 TDS produced classification rules that were applied to the 10,000 scores and plotted to evaluate their performance (Exhibits 29 through 32).

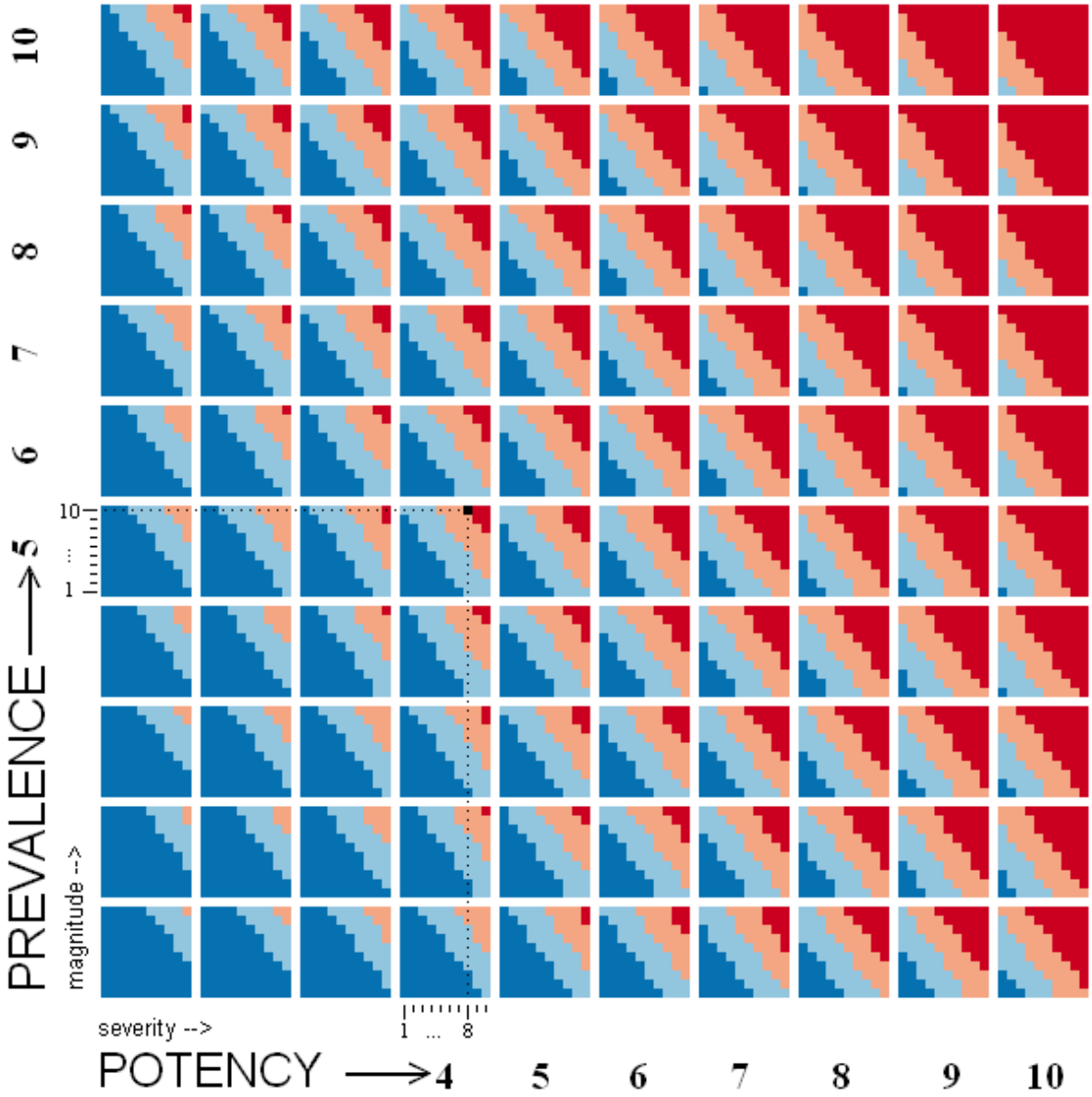
Exhibit 29 is another example of the graphic tool introduced in Chapter 3, Exhibit 19, to help visualize the multi-dimensional space of the CCL classifications. The graphical analysis shows five elements of the model results, the four attributes evaluated and the categorical decision (L, L?, NL?, and NL) in a single graph. Note in Exhibit 29 that the vertical and horizontal axes show two attributes on each axis. The attribute scores for Potency are the large squares across the horizontal axis. The corresponding score for Severity for each Potency score is a separate scale within each larger square. That is, each Potency square has a range of Severity scores. Similarly the Prevalence and Magnitude scores are plotted on the vertical axis with Prevalence along the primary axis and Magnitude along the axis imbedded in each Prevalence square. The categorical decision assigned to each potential attribute score combination is color coded. Red represents a L decision, peach, a L?; light blue represents a NL? and dark blue represents a NL decision.

Exhibit 28. Summary of Individual Quaternary Model Classifications

(shaded cells are exact match with Expert Decisions)

Consensus Blinded Decisions	**Model Decisions**			
	ANN			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	37	5	0	0
3 (L?)	5	44	7	0
2 (NL?)	0	6	53	6
1 (NL)	0	0	5	34
	CART			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	26	12	4	0
3 (L?)	1	47	8	0
2 (NL?)	0	9	53	3
1 (NL)	0	0	8	31
	Linear			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	26	16	0	0
3 (L?)	1	47	8	0
2 (NL?)	0	6	54	5
1 (NL)	0	0	7	32
	MARS			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	37	5	0	0
3 (L?)	10	30	16	0
2 (NL?)	0	3	59	3
1 (NL)	0	0	6	33
	QUEST			
	4 (L)	**3 (L?)**	**2 (NL?)**	**1 (NL)**
4 (L)	42	0	0	0
3 (L?)	13	41	2	0
2 (NL?)	0	8	54	3
1 (NL)	0	0	2	37

Exhibit 29. ANN Model Predictions for the Four Attribute Space (10,000 possible score combinations)



The colors represent the classification decision: List = red; List? = beige; Not List? = light blue, and Not List = dark blue. One TDS contaminant (Potency = 4, Severity = 8, Prevalence = 5, and Magnitude = 10) is shown in black, though the workgroup's decision for that contaminant is List (red). This particular contaminant is always shown in contrasting color to help the viewer orient to the details of the graph and check the scaling and axes.

[1] Expressed in RGB format, dark blue is (5 113 176), light blue is (146 197 222), beige is (244 165 130), and red is (202 0 32). These colors were selected using ColorBrewer, by Cynthia A. Brewer of Penn State University. ColorBrewer can be found online at www.ColorBrewer.org.

Exhibit 29 plots the results of the ANN models classifications for the 10,000 combinations of attribute scores. The patterns clearly show a logical progression from the lower left to upper right, progressing from Not list predictions (dark blue) for low attribute scores, through NL? and L?, to List classifications for the highest scores, both within each square and across the entire matrix. The graphical analysis helped to understand and visualize the logic of the discriminant approach of models and to visualize the performance with the TDS. The QUEST model produces a very similar graphic result to the ANN model.

In contrast to Exhibit 29, Exhibit 30 shows the MARS results. The figure shows areas where red (L) directly touches light blue (NL?) and where dark blue (NL) touches beige (L?). Both are indications that the model was unable to define the intermediary categories. Another problem can be seen in the lower right box of the figure, where Potency is 10 and Prevalence is 1. Within that box, when magnitude is 1(along the bottom edge of the box), as Severity increases, the decision can be seen to go directly from NL? to NL (light blue to dark blue). This unacceptable result also occurs for several other combinations of high Potency and low Prevalence. These results were not considered logical or acceptable by the EPA workgroup. Exhibit 31 shows that the univariate CART model exhibited similar problems.

The adapted Linear regression model, shown in Exhibit 32, presents an interesting variant. As noted, the Linear model predicts average classification of contaminants. In other words in contrast to ANN or QUEST which predict a classification as an integer of 3 (or L?), the Linear model predicts the value from the regression model, such as 3.312 (rounded to 3 = L?), so the colors can be displayed more as a continuous variable. The Linear model again displays a very logical function across the total attribute space.

As discussed above, the CART and MARS models exhibited inconsistent categorization of contaminants and poor performance in the decision matrix comparisons, while the other three models (ANN, Linear, and QUEST) performed very well with respect to TDS error loss, number of training set errors, and the logic of the classification model. The linear model was generally able to predict the workgroup average within approximately 0.3 (less than half a category). Hence, evaluating ways to apply the model results focused on procedures for utilizing the results from the ANN, Linear, and QUEST models.

Exhibit 30. MARS Model Predictions for the Four Attribute Space (10,000 possible score combinations).

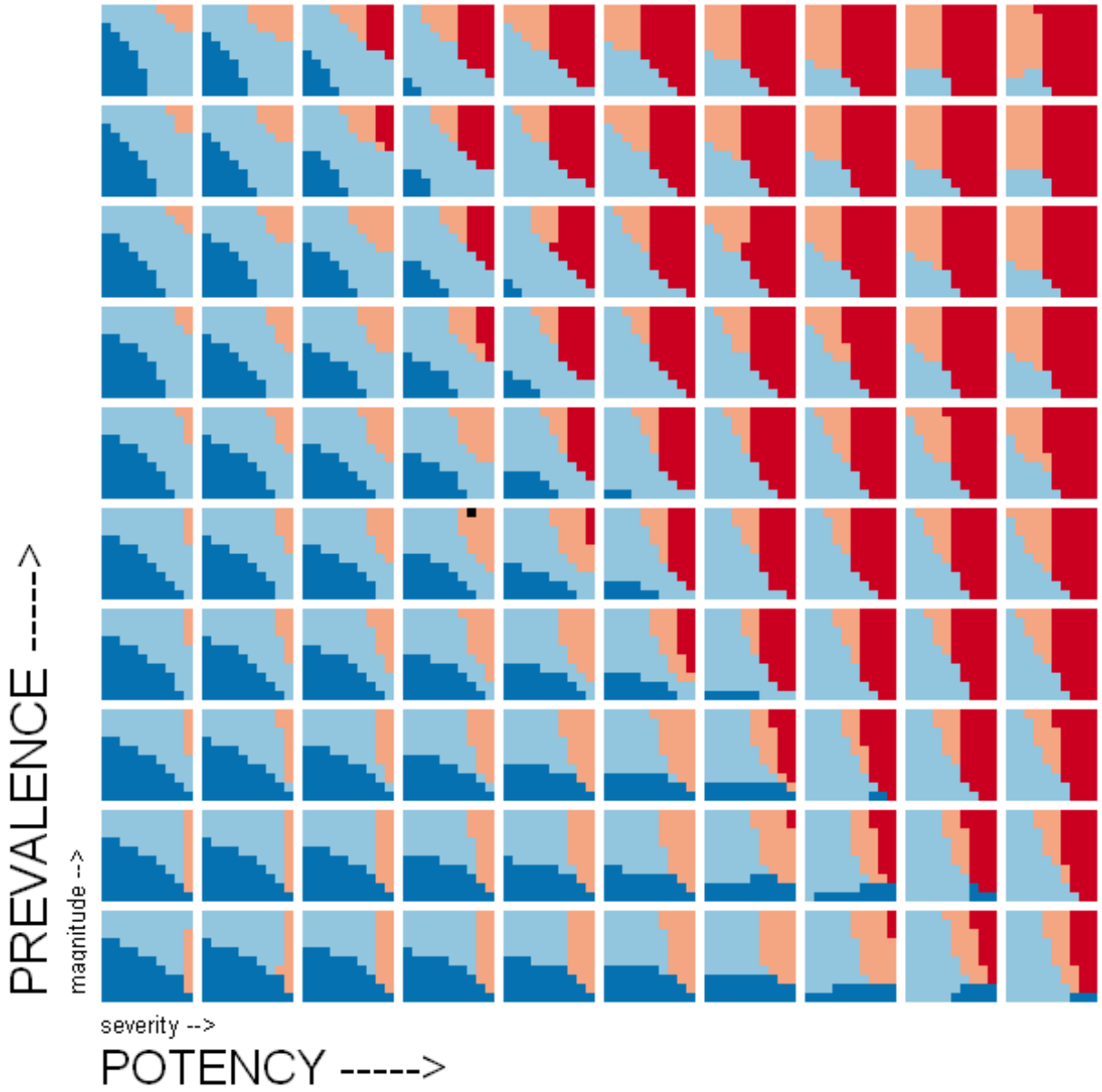
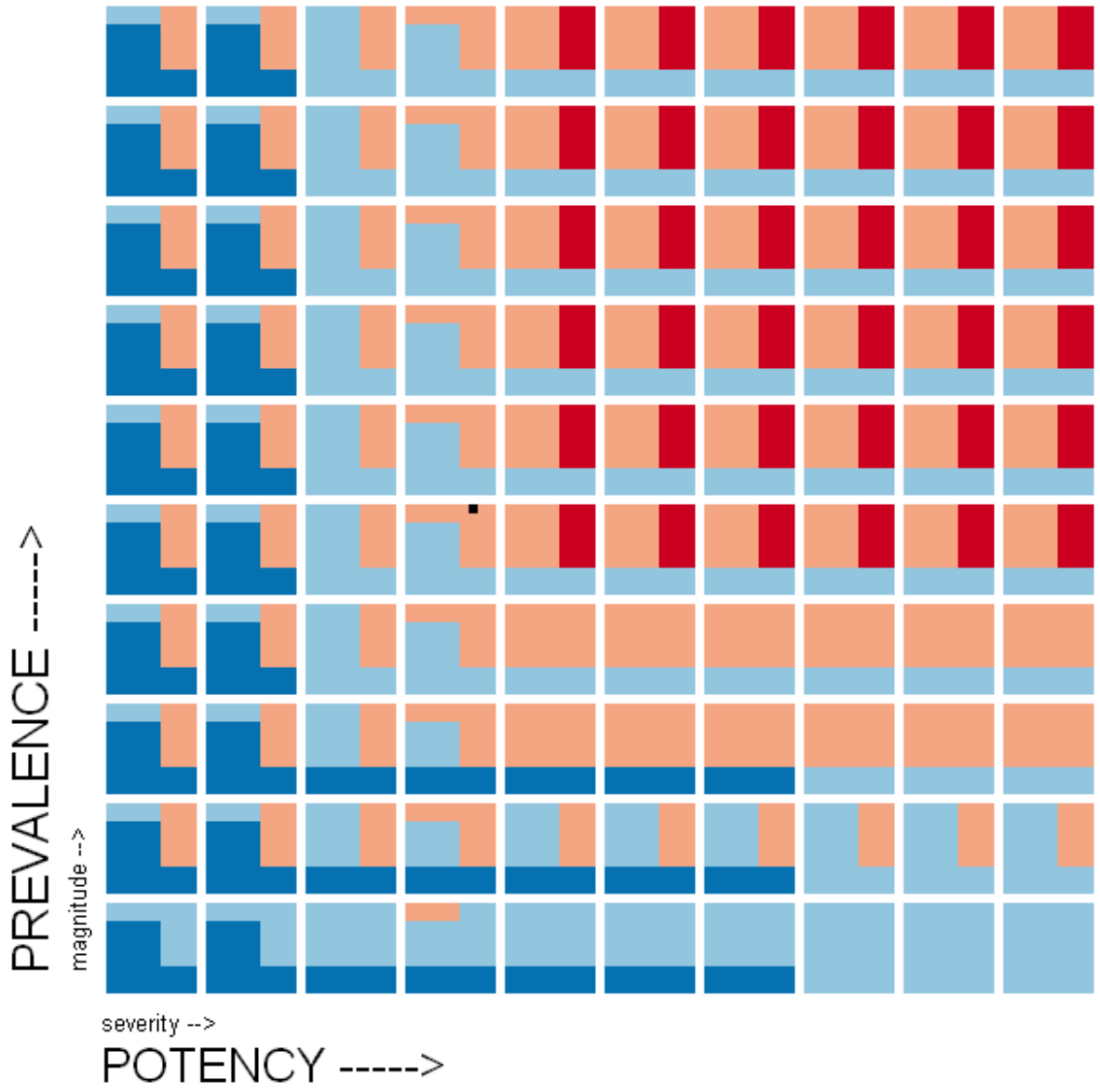
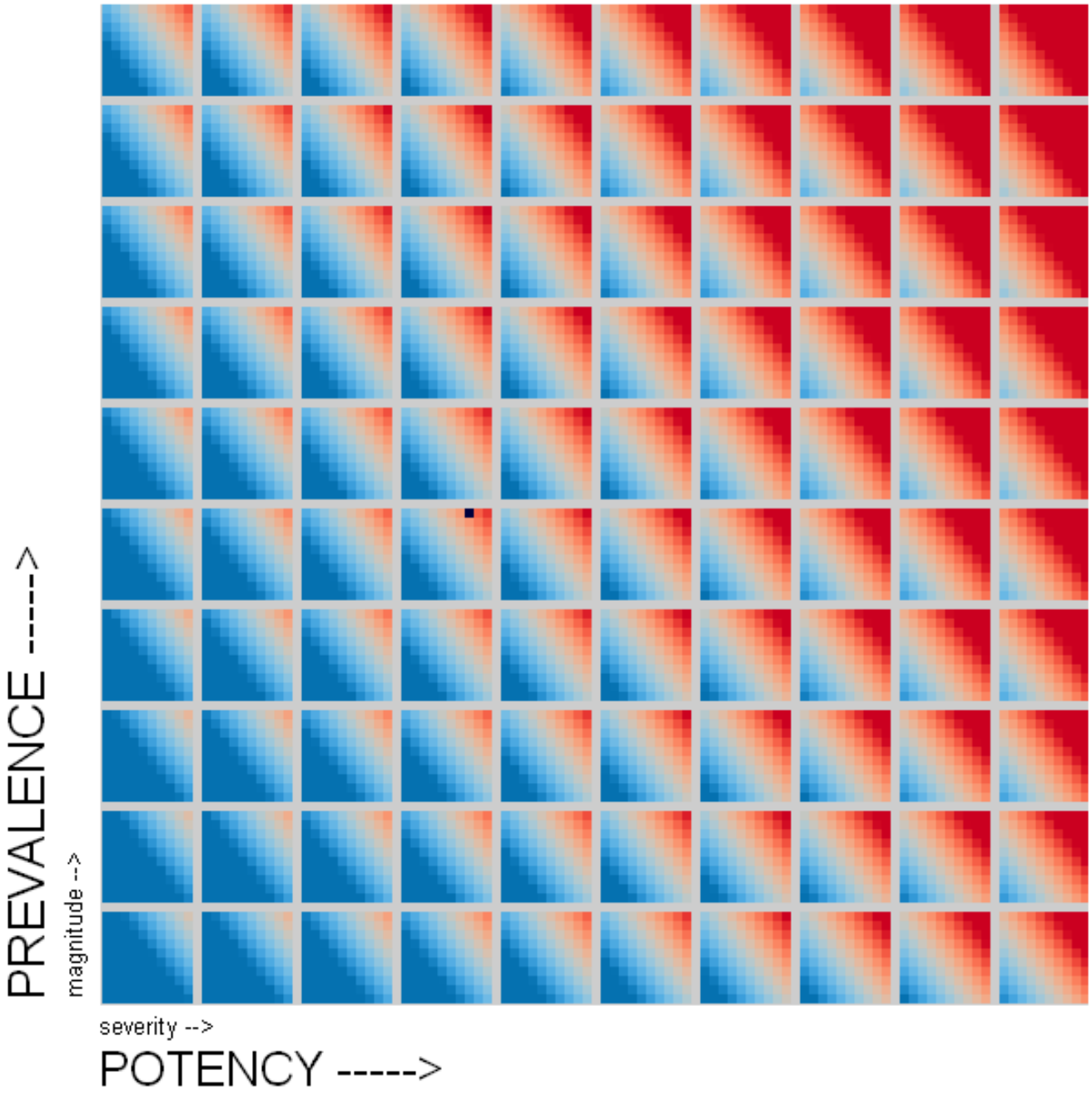


Exhibit 31. Univariate CART Model Predictions for the Four Attribute Space
(10,000 possible score combinations)



See Exhibit 4-7 for the key and text for discussion.

Exhibit 32. Linear Model Predictions for the Four Attribute Space (10,000 possible score combinations)



4.5 Applying Model Results

From the inception of the development of the CCL classification process, EPA intended to use classification models as decision support tools. It was envisioned that, after testing and evaluation, a model(s) might be used to process complex data in a consistent, objective, and reproducible manner and provide a prioritized listing of candidate contaminants for the last stage of the CCL process, an expert review and evaluation. This also would help to focus resources for the review and evaluation of potential contaminants. The use of classification models as a tool in the CCL process is a new approach, a new application of such tools.

Several factors have been considered in assessing how to utilize the model results. After testing, EPA determined that three models performed well: the ANN, Linear, and QUEST models. These are three different classes of models, with three different mathematical approaches, but all provided similar results and logical determinations. Yet the results of each are unique (e.g., Exhibits 29 and 32). Therefore, EPA explored simple ways to combine the results of all three models, to capture both agreement among models and unique results. Two straight forward approaches looked most useful and were applied: a simple additive approach, and a collective rank-order approach.

4.5.1 Additive Model Results

The first step in combining the results of the three models was to simply add the results of their classifications for each contaminant. A tabulation of all contaminants (in the TDS) was prepared with their predicted classification from the models. Recall, the model output is as a class (number), with 4 equaling L through 1 equaling NL. The Linear model output was rounded to its integer class for this approach). Then the 3 results were simply added. This resulted in 10 "bins" or classes, ranging from 3 (all three models classed the contaminant as a 1) to 12 (all three models classed the contaminant as a 4). Hence, a contaminant with an additive score of 11, had two models class it as 4, totaling 8, and one model class it as a 3. A comparison of the sum of the three models to the TDS workgroup Decisions is shown in Exhibit 33.

Exhibit 33, shows some important features of the additive process. For 142 of the 202 contaminants, the three models were unanimous and in agreement with the TDS. Every contaminant that the subject matter experts classed as List (by consensus) was predicted as a List by at least one model. The models do move some NL? into a strong L? positions, but only 2 of the L? contaminants were placed into the NL? category. The areas where the models differ in outcome can provide a place to focus some review during the development of future CCLs.

4.5.2 Additive Rank Order Results

To provide a different approach from the 10 additive classes, a simple method to provide a more continuous rank-order was also developed. The output for each model was used to produce a rank-ordering for that model; ordering from highest (a L candidate) as number one, to lowest (a NL) as number 202 for the TDS. Once the ranks for a model were ordered, the contaminants were simply assigned a number from 1 to 202 (high to low). After this was done for all three models, the rank numbers were added (resulting in a range from 3 to 606) divided by 3 (just to stay on the 202 scale), and then reordered by their composite ranks.

Exhibit 33. Summary Comparison of the Sum of the 3 Model Decisions to the Distribution of the Workgroup Blinded (TDS) Decisions

		Consensus Blinded Decision			
Sum 3 Model Results		**4 (L)**	**3 (L?)**	**2 (NL?)**	**1 (NL)**
All 3 = 4 (L)	**12**	**26**	1		
	11	11	4		
	10	5	8		
All 3 = 3 (L?)	**9**		**35**	6	
	8		1		
	7		5	2	
All 3 = 2 (NL?)	**6**		2	**49**	2
	5			4	3
	4			2	2
All 3 = 1 (NL)	**3**			2	**32**
Sum		42	56	65	39

Shaded cells are unanimous model decisions that match with the TDS. These analyses were also conducted using all models. The analysis reinforced some of the problems discussed for the CART and MARS applications.

As part of the unique input of the three models, each model produces different output with which to develop its own prediction and a rank-order. The Linear regression model as applied, predicted the outcome as a continuous variable from the regression equation (e.g., 3.312), and these values were simply used to rank-order. ANN produces a probability of a contaminant being a 4. So, for ANN, the probabilities for each contaminant were used for the rank-ordering. QUEST does require some processing after the model produces classification predictions to produce a rank order. For QUEST, the distance from the lower discriminant surface was computed. The contaminants were then rank-ordered within a classification group (i.e., ranked within the L? group), then a composite was compiled. QUEST, as a classification decision or regression tree, produces more ties than the other models, but it still produces enough of a continuum that it did not present a problem.

The composite provides a nearly continuous rank-ordered list that can further help to prioritize the analysis for the expert review. Combining the additive results and the rank ordering could also be useful. Knowing which contaminants get unanimous 4s and 1s, or identifying contaminants that stand out as anomalies in one model was useful in the review of the model output. Having the rank-ordering within the group that included a L? decision, for example, was useful for prioritizing additional evaluation.

5.0 MODEL OUTCOME AND POST MODEL EVALUATION PROCESS

The preceding chapters have described the process that was developed for selecting the CCL from the PCCL. The companion document, *CCL 3 Chemicals: Screening to a PCCL* (USEPA, 2008b), describes the approach that was used for screening and selecting the PCCL from the Universe of chemicals. Once the PCCL screening was executed, the Attribute Scoring Protocols finalized, and the models trained, all of the PCCL chemicals were scored for their attributes and run through the models. This chapter describes the results from the modeling and the processes EPA used in evaluating the model output before selecting the preliminary CCL 3.

The evaluation of model output lead EPA to formulate several post-model refinements that were added to the CCL selection process, including an approach for considering the certainty reflected in the differing data elements. The post-model analyses are also described in this Chapter.

5.1 PCCL Characterization and Model Results

The screening process, described in *CCL 3 Chemicals: Screening to a PCCL* (USEPA, 2008b), selected the chemicals for the PCCL. The attributes for these chemicals were scored using the procedures presented in Chapter 2 and evaluated by the three models described in Chapter 4. Exhibit 34 illustrates the results of the model output for the PCCL contaminants[8]. The PCCL consisted of chemicals with variable health effects data, ranging from RfDs to Lethal Dose 50 (LD_{50}), and occurrence data, ranging from measured water concentration data from PWSs to production volume data.

Exhibit 34. Model Results for the PCCL Chemicals

3 - Models Decision	% of PCCL	Total # PCCL	Finished or Ambient Water	Release	Production
L	9%	**44**	3	24	17
L-L?	12%	**58**	9	29	20
L?	33%	**163**	26	64	73
NL?-L?	6%	**30**	6	11	13
NL?	28%	**139**	29	28	82
NL?-NL	4%	**20**	7	9	4
NL	9%	**46**	21	7	18
N(all)	100%	**500**	101	172	227

As described in Chapter 4, three models were used in classifying the PCCL contaminants. The bolded decision category (i.e. L, L?, NL?, NL) in Exhibit 34 signifies that all of the models were in 100% agreement with that listing decision. The other categories (e.g., NL?-NL) represent varied agreement where one or two of the models choose one listing option and one or two

[8] The screening of the CCL 3 Universe, including processing with supplemental data during the nominations process, resulted in 532 chemical contaminants for the PCCL. These chemicals were scrutinized as part of the classification and modeling process. Some of the PCCL chemicals had limited data available for scoring and could not be run through the models process. The 32 contaminants that had limited data remain on the PCCL. They are identified in Appendix G. Exhibit 34 recaps the model output for the 500 chemicals that were scored and processed.

models chose a different option. None of the models categorized a contaminant in a category more than one category higher or lower than the other models. That is, no contaminants were categorized as an "L" by one model and as an "NL?" by another model, or vice versa. The models categorized approximately ½ of the chemicals on the PCCL as L? or above. When analyzed by data type, the majority of chemicals in the List category had LD_{50} data for health effects. This was a concern and became an important issue for consideration in the post-model evaluation process.

5.2 Evaluation of the Modeling Output

As part of the last stage in the CCL classification process, the model output was reviewed by internal EPA experts. This step involved:

- a more detailed review of the data used,
- a review of supplemental data, and
- deliberations on how the model data should be used to produce a draft proposal for a CCL.

Specifically, the function of the team was to critically compare the results from the model to the information in the database dossier for the individual chemicals, and identify any concerns with the model output. This exercise was conducted for a cross section of the model outcomes and their associated contaminants.

The Evaluation Team was comprised of the participants (EPA scientists, engineers, and environmental protection specialists from the OW, Office of Research and Development, Office of Children's Health, and Office of Pesticide Programs). The Evaluation Team met on a weekly basis for approximately 8 weeks to discuss the evaluation results.

5.2.1 Procedure

Prior to the initiation of the evaluation effort, all Evaluation Team members received background descriptions of the CCL process for chemicals (chapters 1-4 of this document), Attribute Scoring Protocols, and evaluation work sheets. A spread sheet with the attribute scores, the data that supported the scores, and the model output for each of the chemicals selected for the first review session was also included in the package. An initiation meeting was held to familiarize the participants with the contents of their evaluation package and discuss the approach that would be followed in evaluating the model output for individual contaminants.

Participants on the Evaluation Team received a set of contaminants and their data dossiers for evaluation. The completed evaluation sheets were submitted so that the results could be compiled for discussion. The evaluation sheets allowed the participants to:

- Comment on the model input data for each attribute
- Provide a statement on their level of confidence in the data underlying each attribute score
- Express agreement or disagreement with the model output
- Indicate their degree of confidence in the model decision
- Provide an explanation for their agreement of lack of agreement with the model decision.

Following submission of the evaluation results for each set of contaminants, the Evaluation Team discussed the outcome of the evaluation, concentrating first on those contaminants with the greatest differences among the reviewers. These discussions identified the issues and steps described in the following sections of this chapter. The Evaluation team reviewed a subset of 129 chemicals from the PCCL. The contaminants were divided into groups as follows:

- Contaminants with finished and/or ambient water data
- Contaminants with release data (pesticide applications and/or TRI), and
- Contaminants with production data.

The team evaluated all contaminants with finished and/or ambient water data and a randomly chosen subset of the contaminants with release or production data. The identities of the contaminants were blinded for the review. This was done so that the team would focus their review on the data for a contaminant and not its name. The identity of all contaminants was revealed when the team discussed the evaluation results.

5.2.2 Evaluation Results

Discussion of the model results raised issues that are important to the selection process for CCL 3 and subsequent CCLs. The evaluators represented a variety of disciplines and contributed important perspectives reflecting their field of specialization. Below are some of the important issues that were raised by evaluators:

- The ratio between the health reference value and the concentrations observed in finished and/or ambient water is an important relationship that is not entirely captured by the four attribute scores. When finished and/or ambient water data were available, this ratio was most often the reason for not agreeing with the model output. For example, the model may have classified a chemical as an L?, but when the health value and concentration data were compared, the outcome indicated that occurrence was one or more orders of magnitude below the health-based benchmark. In this situation, the evaluators usually disagreed with the models decision.

- Confidence in the data elements used for attribute scoring varied widely among the PCCL contaminants. Evaluators noted that there was a considerable difference in the weight-of-evidence for the differing types of data used to score PCCL contaminants. Although the scores used a hierarchy in selecting the data elements that best represented health effects and occurrence, the most highly ranked data element was not equivalent for every chemical. Individual chemicals used different combinations of data. The type of data elements used to represent the occurrence and health effects became a subject of

discussion for the Evaluation Team. Some contaminants had recent UCMR monitoring data combined with an Office of Pesticide Programs (OPP) RfD and others had TRI release data combined with an LD_{50}. For some chemicals, the best data came from an LD_{50} combined with the number of pounds produced per year and environmental fate properties. The evaluators were more comfortable with the model decisions based on strong supporting data than on those based on weak data sets.

- Reviewers felt it was important that the occurrence and health values represent the same form of the chemical. This is particularly important for nonmetals where the common inorganic form of the element is a complex ion (i.e. phosphate) and not the element (i.e. phosphorous). This is also important for metals where the occurrence data represent ions in solution that may have been paired with a toxicity value for the free metal.

- Toxicity data from National Cancer Institute/National Toxicity Program bioassays were incorporated into the Universe for a number of contaminants that were positive for tumors, and were tested by way of the inhalation route of exposure. Some of these contaminants were screened to the PCCL on the basis of their qualitative cancer findings. They were scored for Potency and Severity based on slope factors that had been derived for the oral route of exposure, but based on the inhalation data without the use of Physiologically Based Pharmacokinetic (PBPK) modeling. Some of these very volatile contaminants received L or L? model designations. Reviewers questioned whether toxicity data from inhalation studies should be used for scoring cancer Potency. Therefore, only cancer slope factors that were derived using PBPK modeling for cross route extrapolation were used to score chemicals. Inhalation data were not used for non-cancer endpoints.

- Due to the risk assessment policy differences between agencies, the hierarchy for scoring Potency and Severity considered the agency that established the value. However, some reviewers questioned whether the date of the assessment rather than the Agency conducting the assessment should be the basis for the hierarchy.

- Prevalence and Magnitude were given the lowest possible scores ("1") when a contaminant had been monitored but there were no detections. Since the detection level for a few chemicals was above the health-based value, some reviewers questioned whether this was appropriate. They suggested that it might be better to use the detection limit as the basis of the Magnitude attribute score.

- UCMR 1 screening studies monitored a small number of statistically selected sites (300). There were cases where there were no finished water detections in the screening surveys, but the same contaminant had been detected in ambient water by USGS. Reviewers questioned the placement of finished water above ambient water in the hierarchy in these cases.

- A number of disinfection byproducts (DBPs) had occurrence data based on production or release, while some had no occurrence data. Production and release data do not

adequately represent the potential occurrence of DBPs and byproducts of other treatment processes in finished water.

- Reviewers were uniform in feeling that contaminants that had a Potency score based on an LD_{50} value and a Severity score of 9 (death), should be returned to the Universe independent of their other attribute scores.

The quantitative results of the model output evaluation are summarized in Exhibit 35
For Exhibit 35, agreement with the model outcome by a majority of the Evaluation Team constitutes agreement. Appendix F lists the chemicals reviewed by the Team and the percentage of the team agreeing with the model outcome for the individual chemicals.

Exhibit 35. Results of the Model Output Evaluation (Total = 129 chemicals)

	Finished/Ambient Water Grouping	Release Grouping	Production Grouping
Number of Contaminants	89	28	12
Agreement with model outcome (>50%)	96%	89%	67%
% where an outcome higher than the model was recommended	2%	0%	0%
% where an outcome lower than the model was recommended	2%	11%	33%
% high confidence decisions (avg.)	36%	16%	7%
% medium confidence decisions (avg.)	49%	31%	17%
% low confidence decisions (avg.)	15%	52%	76%

5.3 Post-Model Adjustments to Output

Based upon issues identified by the Evaluation Team comments, several post-model refinements were added to the CCL process. The post-model refinements changed the standing of some of the chemicals as candidates for CCL 3. The post-model adjustments that were incorporated are discussed in the following sections.

The simplest of the post-model adjustments was the review of the coupling of occurrence data with toxicological data for the inorganic contaminants. This problem was a result of some data being reported for the element of interest (and its CAS number) and other data being reported for one or more ions and/or salts that contained the element.

5.3.1 Using Supplemental Sources to Identify the Data Most Relevant to Drinking Water

One issue identified by the Evaluation Team was that scoring should be based on the data most relevant to exposure from drinking water. For example, DBPs were included in the Universe and many were brought forward to the PCCL. The data used to score these contaminants for occurrence should be based on their occurrence in drinking water at PWSs, not ancillary data that may be available such as release or production volume. There are DBP data from the

Information Collection Rule monitoring and supplemental studies identified in the CCL Nominations process, These data had not originally been included in the data used for scoring Prevalence and Magnitude. As part of the post-model processing the data were retrieved, scored and the chemicals were modeled using the supplemental data. For future CCLs some of these supplemental data sources may be included in the Universe and used in the attribute scoring rather than as a post- model adjustment.

5.3.2 Calculation of a Health-Concentration Ratio for Contaminants with Water Data

The models classified chemicals using scores for the four attributes. The Evaluation Team recognized that the relationship between Potency and Magnitude was important when deciding whether or not to list a chemical, but only when the Magnitude data represented concentration in ambient or finished water. Accordingly, calculation of the ratio between the health-based value and the 90th percentile concentration in finished or ambient water was added as a post-model process. EPA also sought methods that could be used to model concentration data to develop a similar ratio for contaminants that did not have direct measurements in water sources. The health/concentration ratio serves as a benchmark that suggests concern for a contaminant when it is low, and lesser concern when it is high.

5.3.2.1 Developing a Health Reference Level (HRL)

To calculate the health-concentration ratio, the data that provided the Potency score were converted to the HRL benchmark that the Agency has used for Regulatory Determination. For a carcinogen, the HRL is the one-in-a-million cancer risk expressed as a drinking water concentration. For non-carcinogens, the HRL is equivalent to the lifetime health advisory value. The lifetime health advisory value is obtained by multiplying the RfD times 70 kg, dividing by a water intake of 2 L/day and multiplying by a 20% relative source contribution (unless there are data to suggest that the 20% is inappropriate).

Determining the HRL for chemicals where the Potency value was the NOAEL, LOAEL, or LD_{50} value from an individual study, required application of an uncertainty factor to adjust the toxicity value to an RfD approximation. In these cases, the uncertainty factor was based on the difference in the modal values from the log-based data distributions used to develop the Potency scoring equations (see Chapter 2). The uncertainty factors applied are as follows:

NOAEL – 1,000
LOAEL – 3,000
LD_{50} - 100,000

The NOAEL and LD_{50} uncertainties were derived from the difference in the constant for the non-cancer Potency scoring equation (Exhibit 4). For a NOAEL, the difference is 3 (7 – 4 = 3) or 1,000 since the Potency equation is log based. The difference for an LD_{50} is 5 (7-2 = 5) or 100,000. The uncertainty factor (3,000) chosen for the LOAEL is a half log greater than that for the NOAEL, in recognition that the LOAEL is a level that causes effects rather than no effects.

5.3.2.2 Developing a HRL – Concentration Ratio

The 90th percentile (of detections) water concentration was selected as the point of comparison for the ratio, rather than the mean or median. The CCL list is designed to identify contaminants that may benefit from a Health Advisory, even if they do not merit a positive regulatory determination. The 90th percentile concentration level was used as a conservative benchmark that may identify a possible need for a health advisory for areas of the country that may have higher concentrations in drinking water than others.

The ratio of the heath-value to the 90th percentile concentration detected in water (either ambient or finished) was calculated for all contaminants with water data. If the ratio was 10 or less the contaminant was selected for consideration for the draft CCL 3. If the ratio was greater than 10, the contaminant was eliminated from consideration for CCL 3 and remains on the PCCL. For chemicals that had been monitored but not detected, and for chemicals that were detected in ambient waters but not finished water, analytical method detection limits were compared to the HRL to ensure that the detection accounted for the health effects. Consideration was also given to whether the ambient water data suggested that the UCMR 1 screening might have been too limited to identify the contaminant in areas where it might pose a problem. For contaminants that had limited finished water data, but more robust ambient water monitoring data, the ambient water concentration was used to develop the ratio.

5.3.2.3 Developing a Ratio for Contaminants Without Concentration Data

OW worked with the OPP to obtain supplemental modeled data on the levels of pesticides projected to be found in surface and ground water. The modeled concentrations of pesticides in water are included in the OPP registration and re-registration evaluation documentation, but they are not readily available in a form that could be used for the Universe database. Once this data gap was identified, OPP shared the data with OW and they were evaluated in the post-model process.

For pesticides, the modeled data from OPP were compared with the health reference level. As part of the pesticide registration process, EPA calculates an Estimated Environmental Concentration (EEC) in water or Estimated Drinking Water Concentration (EDWC) depending on the year the last assessment was completed. Both the EEC and EDWC are derived from models that estimate the pesticide's concentration in an index reservoir used for drinking water. OPP used the PRZM-EXAMS model for surface water. Ground water concentrations are derived using the SCI-GROW regression model to represent exposures in shallow ground water. Both the EEC and the EDWC are equivalent. The modeled EEC values allowed EPA to calculate the HRL/EEC or EDWC ratio for pesticides and/or their degradates. Pesticides with HRL/EEC ratios of 10 and lower were selected for the draft CCL 3.

5.3.3 Grouping Contaminants based on Data Certainty

Data certainty was not directly factored into the development of the attribute scoring protocols, but was indirectly factored into the protocols through the use of the hierarchies of the data used for health effects and occurrence (Chapter 2). In the evaluation of the model output, data certainty was an important factor for the Evaluation Team. In cases where the model output listed a chemical with data from high in the hierarchy (e.g. IRIS RfD, UCMR/NAWQA

concentration), the team typically agreed with the model decision. The Team confidence ranking for model decisions based on data from high in the hierarchy was generally high while confidence for data from low in the hierarchy was generally low (see Exhibit 35). Accordingly, as part of the post-model evaluation process, EPA tried various approaches for addressing the certainty issue.

Initially, OW attempted to develop numeric certainty scores for each data element, but decided not to use this approach because the certainty scores could not be calibrated due to the subjectivity in assigning the numeric values. For example, it would be difficult to justify that a chemical evaluated by environmental release data should be assigned a certainty score of 6, while a chemical evaluated by production volume should be assigned a certainty score of 10 versus 9. Therefore, OW decided to place tags on the chemicals that characterize the certainty. The chemicals were tagged as high, medium and low certainty based on the combinations of data elements that were used to score the attributes for health effects and occurrence. The certainty tags are not calibrated measures of certainty. They were developed to express the relative certainty associated with the data elements that were used to score a chemical's attributes. The certainty rankings assigned to the combinations of individual attribute data elements are listed below:

High Certainty:
Finished Water + RfD/ CSF, NOAEL or LOAEL
Ambient Water + RfD/CSF, NOAEL

Medium Certainty:
Ambient Water + LOAEL
Release/Application + RfD, NOAEL, LOAEL
Production + RfD

Low Certainty:
Finished Water, Ambient Water or Release/Application + LD_{50}
Production + NOAEL, LOAEL, LD_{50}

The high certainty bin consisted of chemicals that had been scored based on the most relevant data for occurrence in water and with the richest database for health effects. Such contaminants are expected to be good candidates for regulatory determination with minimal research needs. Examples of chemicals in the high bin include chemicals with reference doses and measured water concentration data. The medium bin consists of chemicals that need further occurrence and/or health effects research. These include chemicals that may have well studied health effects data but may need additional occurrence data (e.g. chemicals with release data but, no measured water occurrence data). The low certainty bin consists of chemicals that need extensive health effects and occurrence research that may take longer than the life cycle of a CCL. Examples include chemicals with LD_{50} and/or production volume data. The CCL should consist both of chemicals that provide sufficient data to support regulatory determinations, as well as chemicals that are of concern and need to be targeted for additional drinking water research. Contaminants from each bin were scrutinized separately in selecting which ones should be listed on the CCL 3.

5.3.4 LD_{50} Values with Limited Documentation

Following the advice from the Evaluation Team, Severity scores based on death from LD_{50} studies were removed from the modeled PCCL results. This decision applies to contaminants where no critical endpoint other than death was specified in the source of the LD_{50} data. These contaminants were removed from consideration for the CCL. None of the chemicals with LD_{50} derived health attributes had ambient or finished water data.

5.4 Selecting the Draft CCL 3

The chemicals for the preliminary CCL 3 were selected from within the three uncertainty bins, described in Section 5.3.3, with the emphasis placed on the source of the occurrence data (e.g. measured water concentrations, release, and production). Four groups of chemicals were placed on the draft CCL 3 based on their modeled scores, the potency-concentration ratios analysis, where available, and the estimate of data certainty. They included:

- 36 chemicals in the high certainty bin, which have finished water data and an HRL/90th percentile concentration ratio of ≤ 10.
- 24 pesticide chemicals in the medium certainty bin, which have modeled surface and/or ground water data that yielded a HRL/concentration ratio of ≤ 10
- 27 chemicals in the medium certainty bin, which have release data that gave modeled L or L? rankings
- 8 chemicals in the low certainty bin that were nominated and reviewed with supplemental information that was submitted, were selected for the CCL.

No chemicals with only LD_{50} and production data were selected for the CCL. These chemicals are viewed as candidates for research and consideration for later CCLs.

Subsequent to placement on the preliminary CCL 3, the list was subject to review by a panel of qualified external experts and stakeholders. Stakeholder input was considered in determining which chemicals from among a preliminary CCL 3 grouping were retained for the proposed CCL 3. After publication of the CCL 3 Proposal, EPA will seek consultation from the Science Advisory Board and consider additional stakeholder comments on the Federal Register proposal, before finalizing CCL 3.

5.5 Summary

The Draft CCL 3 and the process used to select contaminants was developed and tested to meet the Safe Drinking Water Act requirements and address recommendations and advice from the NRC (2001) and NDWAC (2004). The Agency has developed a draft CCL 3 that:

- Considers of a broad Universe of contaminants
- Relies on best available science and information to inform the process
- Evaluates the known or potential health effects and occurrence in screening the Universe to a PCCL

- Uses a set of contaminant attributes and prototype classification algorithms as decision support tools in selecting candidates for the CCL from the PCCL
- Provides an opportunity for nominations and expert judgment.

The first application of the CCL 3 process accomplished many of the specific recommendations from NRC and NDWAC. During the development of CCL 3, the Agency identified areas for improvement that can be implemented in the selection of CCL 4 and later CCLs.

6.0 REFERENCES

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7.0 APPENDICES

Appendix A. Attribute Scoring Protocols

This section provides scoring protocols for the health effects attributes of Potency and Severity as well as the Occurrence attributes, Magnitude and Prevalence.

A.1 Potency Scoring Protocol

This section describes the process for assigning a numerical score for the Potency attribute.

Protocol for Potency Scoring

Step One: Open the spreadsheet for Potency and Severity Scoring (a sample of this spreadsheet is shown in Exhibit A.1) and is an alternative to using the computer version of the spread sheet.

Step Two: Enter the name of the chemical in the column labeled contaminant.

Step Three: Identify and score highest-ranked non-cancer data element for potency using the following hierarchy of values:

Reference Dose (RfD) or equivalent > No-Observed-Adverse-Effect Level (NOAEL) that is lower than the lowest LOAEL > Lowest-Observed-Adverse-Effect Level (LOAEL) > Toxic $Dose_{LO}$ (TD_{L0-} RTECS) > Lethal dose (LD_{50})

- Measured > Modeled

For RfDs (or equivalent) only:

- EPA RfD > ATSDR Minimal Risk Level (MRL) (Chronic> Intermediate >Acute) > RAISHE RfD > Cal EPA Public Health Goal (PHG)[a] > TDIs from WHO/EU/Health Canada > UL from IOM
- Office of Pesticide Programs (OPP) > IRIS for Pesticides

Step Four: Enter the selected quantitative measure of non-cancer potency into the appropriate column of the spread sheet. Make sure that the units are in mg/kg/day. (The spreadsheet formula produces a score in a corresponding column for the data element on the right side of the sheet.)

Step Five: Select a measure for cancer potency if one is available. The preferable measure will be the 10^{-4} risk concentration in drinking water in mg/L. If the risk is expressed at levels other than 10^{-4}, convert the value to the target risk (10^{-4}). If the cancer potency measure is the slope factor, calculate the 10^{-4} risk concentration using the following equation:

$$10^{-4}\ \text{Risk concentration} = \frac{0.0001 \times 35\ \text{kg/day/L}}{\text{Slope Factor (mg/kg/day)}^{-1}}$$

[a] The California PHG will have to be converted from mg/L to a dose by multiplying it by the [Drinking Water Intake (L) ÷ (the body weight (kg) x Relative Source Contribution)].

Step Six: In a case where the entered potency value is a LD_{50} value that is reported as greater than a particular dose, or as a NOAEL with no LOAEL, decrease the score calculated using the spreadsheet by one integer. Situations where there is a NOAEL with no LOAEL can be identified by the lack of a critical effect, because the NOAEL was the highest dose tested.

Step Seven: Choose the higher of the non-cancer or cancer potency scores as the measure of potency.

Note: if no value for Potency can be found that qualifies for this protocol, please refer the contaminant for expert judgment. The only endpoints that may be applied to this protocol are those listed explicitly in the hierarchy of values. Further, the only endpoints considered as equivalent to an RfD are MRLs from ATSDR, RAISHE RfDs, Cal EPA RfDs, WHO or HC, TDIs, and IOM ULs.

Exhibit A.1. Potency Scoring Table

SCORE	RfD	LOAEL/NOAEL	LD50	Car
10	0 - 0.000000316	0 - 0.000316	0 - 0.0316	0 - 0.00000316
9	0.000000317 - 0.00000316	0.000317 - 0.00316	0.0317 - 0.316	3.17E-06 - 0.0000316
8	0.00000317 - 0.0000316	0.00317 - 0.0316	0.317 - 3.16	3.17E-05 - 0.000316
7	0.0000317 - 0.000316	0.0317 - 0.316	3.17 - 31.6	0.000317 - 0.00316
6	0.000317 - 0.00316	0.317 - 3.16	31.7 - 316	0.00317 - 0.0316
5	0.00317 - 0.0316	3.17 - 31.6	317 - 3,160	0.0317 - 0.316
4	0.0317 - 0.316	31.7 - 316	3,170 - 31,600	0.317 - 3.16
3	0.317 - 3.16	317 - 3,160	31,700 - 316,000	3.17 - 31.6
2	3.17 - 31.6	3,170 - 31,600	317,000 - 3,160,000	31.7 - 316
1	31.7 - >31.7	31,700 - >31,700	3,170,000 - >31,700,000	317 - >317

A.2 Severity Scoring Protocol

The score for Severity is based upon the critical effect associated with the data element (RfD, LOAEL, etc.) used to score Potency. Potency must be scored prior to Severity.

Protocol for Severity Scoring

Step One: Identify the critical effect for the contaminant, based on the data used to score the attribute of potency, and enter it into the severity scoring worksheet (shown in Exhibit A.2). If the contaminant has more than one critical effect all of the listed effects should be included. NOTE: If the critical effect is death and the LD_{50} data element was used to score potency, go to Step Four. If the effects are for a LOAEL from RTECS go to Step Five.

Step Two: Locate the critical effect within the Compendium of Critical Effects Table (see Exhibit A.3) and enter the severity score associated with that critical effect in the severity scoring worksheet. If a contaminant has more than one critical effect, choose the highest of the scores.
NOTE: If the critical effect is not listed in the Table, go to Step Three.

Step Three: If the critical effect is not listed in the Table, the scorer should flag that critical effect as 'not listed.' (Health effects experts should be consulted to score these effects.) Once the effect is scored it should be added to the compendium for future use and consistent scoring.

Step Four: If a critical effect is not available, or is "death," use one of the following options for scoring:

1) Search sources identified as supplemental sources for CCL for additional health effects data that could be used to score potency and severity for the contaminant. If data are found that provide a data element from the potency protocol other than LD_{50} to score the contaminant, then that element can be used for scoring. Sources that may be most helpful in this search include: Hazardous Substances Data Bank (HSDB), International Program on Chemical Safety (INCHEM), and the National Toxicology Program (NTP). The element that is found may be used to rescore the contaminant for potency, and subsequently severity, using the score associated with the critical effect endpoint.
2) Search for an alternative critical effect associated with the LD_{50} determination. Locate the LD_{50} study and search for information regarding the types of effects occurring prior to animal death. If a critical effect other than death is given in the study, it may be used to score the severity of the contaminant. (The potency score is still given by the value of the LD_{50}.)
3) If no additional information can be found, recommend that the contaminant be returned to the Universe.

Step Five If the Potency score is a LOAEL from RTECS, the effects listed represent all effects and

not just the critical effect (s). There are three available options for improving the scoring in this situation.

1. If the RTECS data source is included in the supplemental data, review the supplemental information to identify the critical effect. If the supplemental source includes a NOAEL for the critical effect, replace the LOAEL with the NOAEL and rescore potency if necessary.
2. In cases where the data source for the LOAEL is not in the supplemental data search the supplemental data for an alternative data source. If the data identified provides a NOAEL or LOAEL that is the same or lower than that in RTECS or is from a study of higher quality than the RTECS study , use that NOAEL or LOAEL and its critical effect to score both potency and severity.
3. If it is not possible to find better information in the supplemental data sources score the most serious of the effects listed in RTECS.

Exhibit A.2. Severity Scoring Table

Key	Study used to score Potency	Critical Effect(s) for Severity	Severity Score
1			
2			
3			
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Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
1	**NO ADVERSE EFFECT**	No observed effect(s). No observed adverse effect(s). Absence of effects. No critical effect(s) identified. No effect(s) related to treatment. Absence of biologically significant adverse effect(s). Absence of gross light microscopic histopathological change(s). Excedance of the Taste Threshold
2	**COSMETIC EFFECT** (*Interpretation: Consider those effects that alter the appearance of the body without affecting structure or functions*)	Dental fluorosis. Abnormal appearance. Facial flushing. Flushing. Argyria. Dermal sensitization. Skin pigmentation. Hyperpigmentation. Alopecia. Keratosis.
3	**REVERSIBLE EFFECTS; DIFFERENCES IN ORGAN WEIGHTS OR SIZE, BODY WEIGHTS OR CHANGES IN BIOCHEMICAL PARAMETERS WITH MINIMAL CLINICAL SIGNIFICANCE.** (*Interpretation: Transient, adaptive effects*)	***Growth and Weight Effects*** Decreased body weight and or body-weight gain. Increased absolute organ weights. Increased liver weight. Increased kidney weight. Increased relative organ weight. Decreased relative organ weight. Lower ovarian weight. Decreased maternal weight gain. Increased absolute and relative (to body and/or brain) liver weight. Increased kidney body weight ratio. Increase in spleen weight. Increase in thyroid/body weight ratio. Changes in thymus weight. Decreased body weight. Decreased growth. ***Gastrointestinal Disturbances*** Decreased stool quantity. Osmotic diarrhea. Diarrhea. Nausea. Vomiting. GI irritation. GI disturbances.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
3 (cont.)		***Irritation/Irritability*** Chronic irritation. Maternal hyperirritability. Chronic irritation without histopathology changes. ***Biochemical Changes*** Decreased glucose. Increased blood sugar. Increased enzymes. Increased triglycerides. Increase serum concentration of compound. Clinical serum effects. Alterations in clinical chemistry. Increased serum alkaline phosphatase. Significant elevation of serum calcium levels. Enzyme inhibition, induction, or change in blood tissue levels Decreased ESOD activity. Decrease in erythrocyte superoxide dismutase (ESOD) concentration. Minor alteration in clinical chemistry, e.g., decrease in erythrocyte superoxide dismutase (ESOD). ***Hematological effects*** Hematological effects. Abnormal pigments in blood. Decreased lymphocyte count. Decreased blood counts. Methemoglobinemia. Increased carboxyhemoglobin. Hemosiderosis. Anemia. Normocytic anemia. Iron deposits and elevated Heinz bodies in liver. Decreased hemoglobin and possible erythrocyte destruction. Decreased RBC, packed cell volume, and hemoglobin. Hematologic, hepatic, and renal toxicity as evidenced by a statistically significant decrease in hemoglobin, hematocrit, and RBC levels. RBC and liver effects as evidenced by increase Heinz bodies in RBC. Sporadic decrease in hemoglobin and RBC. Decreased RBC and hematocrit.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
3 (cont.)		***Cholinesterase Effects*** Reversible PChE (plasma) or RBC-ChE inhibition without cholinergic symptoms or signs RBC ChE depression without cholinergic symptoms or sweating. Plasma cholinesterase (ChE) inhibition without cholinergic symptoms or sweating. ***Hormone Changes*** Decrease in T3, T4. Dose-related decrease in T4, T3, and increase TSH. Elevated thyroid stimulating hormone (TSH) concentration. ACTH decrease. ***Cellular Vacuolization*** Mild to moderate vacuolization Tubular epithelial vacuolization. Brain cell vacuolization. ***Additional Effects*** Changes in teeth and supporting structures. Sensory organ effects. Centrilobular eosinophilic liver changes. Possible vascular complication
4	**CELLULAR/PHYSIOLOGICAL CHANGES THAT COULD LEAD TO DISORDERS** (risk factors or precursor effects). (*Interpretation: Considers cellular/physiological changes in the body that are used as indicators of disease susceptibility*)	***Hematological Effects*** Jaundice. Anemia Hemolytic anemia. Erythrocyte destruction. Hemolysis. ***Immunological Effects*** Decreased delayed hypersensitivity response. Decrease in cellular immune response. Decrease in humoral immune response. ***Liver Effects*** Fatty cyst - liver and elevated liver enzymes (i.e., SGPT, LDH). Liver cell enlargement or alteration. Liver cell polymorphism. Proteinuria. Renal cytomegaly. ***Cholinergic Effects*** Cholinesterase inhibition with symptoms. Cholinergic signs or symptoms. ***Other Effects*** Hypothermia Mild CNS Effects

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
5	**SIGNIFICANT FUNCTIONAL CHANGES THAT ARE REVERSIBLE OR PERMANENT CHANGES OF MINIMAL TOXICOLOGICAL SIGNIFICNACE.** (*Interpretation: Consider those disorders in which the removal of chemical exposure will restore health back to prior condition*)	***Increased cholinergic effects*** ChE inhibition with sweating, diarrhea, hypotention, and/or fishy body odor.. RBC and/or plasma acetylcholinesterase (AChE) inhibition with cholinergic symptoms or sweating. Brain acetylcholineesterase inhibition with or without signs or symptoms ***Hematological Effects*** GI bleeding. Coagulation defects. Tendency to hemorrhage. ***Structural Effects*** Rachitic bone. ***Renal Effects*** Renal cytomegaly. Renal effects/toxicity (increased uric acid levels; increased urinary coproporphyrins). Inflammatory foci – kidneys. ***Hepatic Effects*** Liver function tests impaired. Fatty-cyst in liver hemosiderosis. ***Multiple Organ Effects*** Effects on the lungs, liver, kidney, thyroid and thyroid hormones. ***Ocular Effects*** Corneal damage. ***Neurological Effects*** Mild neurological signs. Alteration of classic conditioning. Brain ChE inhibition. Myelin degeneration. CNS depression. Brain/ other coverings- recordings from specific areas of CNS. Tremors. Dyspnea. Changes in motor activity. Hypoactivity. Ataxia.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
5 (cont.)		***Other Effects*** Chronic pneumonitis. Clinical selenosis. Nonneoplastic lesions - splenic capsule. Intestinal lesions. Splenomegaly
6	**SIGNIFICANT, IRREVERSIBLE, NONLETHAL CONDITIONS OR DISORDERS.** (*Interpretation: Consider those disorders that persist for over a long period of time but do not lead to death*)	***Multiple Organ Effects*** Histopathological effects in liver, kidney, and thyroid. Minimal to moderate congestion of liver, kidney, and lungs. Liver and kidney pathology. Kidney and spleen pathology. ***Hepatic Effects*** Hepatic lesions/necrosis. Hepatocyte degeneration. Hepatotoxicity. Liver cell polymorphism. Liver effects/toxicity. Liver lesions. ***Renal Effects*** Atrophy and degeneration of the renal tubules – nephropathy (unspecified). Kidney toxicity. Mineralization of the kidneys. Renal dysfunction. Renal effects/toxicity (increased uric acid levels; increased urinary coproporphyrins). Functional and histopathological effects in kidney. Kidney damage (unspecified). Kidney lesions (unspecified). Impaired renal clearance/function. Tubular epithelial vacuolation. ***Sensory and Neurological Effects*** Significant decrease in brain and brain to body weight ratio. Degenerative changes for brain/ other coverings. Peripheral neuropathy- neuropathy (unspecified). Neurotoxicity. Nerve damage (unspecified). Optic nerve degeneration/ damage. Sensory neuropathy. Minimal lens opacity and cataracts. Nasal olfactory lesions.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
6 (cont.)		***Hyperplasia*** Thyroid hyperplasia. Urothelial hyperplasia. Hyperplasia. Squamous and basal hyperplasia of the forestomach. Epithelial hyperplasia – forestomach. ***Cardiac Effects*** Cardiac toxicity. Cardiomyopathy, including infarction. Vascular complications. Right atrial dilation. Convulsions. Mild histological lesions. ***Other Effects*** Gastrointestinal necrotic changes. Chronic irritation with histopathology findings. Forestomach lesions (unspecified). Organ atrophy. Thyroid effects (unspecified). Spleen toxicity (unspecified). Bladder toxicity (unspecified). Bone marrow toxicity (unspecified).
7	**DEVELOPMENTAL OR REPRODUCTIVE EFFECTS LEADING TO MAJOR DYSFUNCTION.** (*Interpretation: Considers those chemicals that cause permanent developmental effects or that impact the ability of a population to reproduce*)	***Reproductive Organ Effects*** Testicular atrophy/damage. Testicular and uterine effects. Atrophied seminiferous epithelium. Histopathological changes in testes. Lesions observed in reproductive organs. Decreased testes weight and testes to body weight ratio, atrophied seminiferous epithelium; and decreased tubular size in testes. Endometriosis. Decreased tubular size in testes. Decreased ovarian weight and function. Altered cellular foci. ***Maternal Toxicity*** Maternal toxicity. Decreased maternal weight gain.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
7 (cont.)		***Fertility effects*** Spermatogenic arrest. Reduced numbers of corpora allata. Reduced or deformed sperms. Adverse reproductive effects. Reduction in fertility. Decreased fertility index. Decrease in size of litter. ***Growth inhibition*** Reduced offspring weight gain, total litter weight, or litter size. Decreased pup weight Decreased lactation indices. Increased runt incidence. Decreased crown-rump length ***Decreased offspring viability*** Excessive loss of litters Increase in number of stillbirths. Maternal and fetal toxicity. Increased intrauterine death. Decreased pup survival or viability. Increased abortion rate. Increase in number of stillbirths. Increased dead pups at birth. Decreased pup viability index. Parturition mortality. Fetal resorptions. ***Developmental effects*** Fetal toxicity/malformations. Developmental toxicity (skeletal or visceral abnormalities). Delayed ossification. Neurodevelopmental effects. Brain cell vacuolization in neonates. Myelin degeneration. Skeletal or visceral abnormalities (Extra ribs and other measures of sexual maturation). Increased retinal folds in weanlings. Mixed sexual differentiation (i.e., effeminization or emasculanization). Imbalance in sex ratio.
8	**TUMORS OR DISORDERS LIKELY LEADING TO DEATH** *(Interpretation: Considers chemical exposures that result in a fatal disorder and all types of tumors).*	Cancer. Suspected carcinogenicity (including short latency periods and rare tumors). Any type of cancer.

Exhibit A.3. Compendium of Critical Effects Table (from Health Advisories & IRIS) For Scoring Severity

Severity Score	Score Definition	Compendium of Critical Effects
9	**DEATH.**	Increased mortality. Longevity. Mortality. Survival. Decreased survival. Increased mortality. Decreased adult survival. Decreased adult longevity. High incidence of mortality at early age (i.e., 25% to 50% by mid-life) in chronic studies. Maternal death during pregnancy. Reduced longevity. Death.

A.3 Prevalence Scoring Protocol

This section describes how to assign a numerical score for the attribute Prevalence.

Step One: Identify highest-ranked data value

When more than one data value is available for a particular contaminant candidate, use the hierarchy in Exhibit A.4. Use the same type of data to score Prevalence as for Magnitude.

Exhibit A.4. Hierarchy of Prevalence Data Elements

Rank	Prevalence Data Element	Type of Data
1	Finished Drinking Water – Percentage of all Public Water Systems (PWSs) with Detections (If data from both NCOD Round 1 and Round 2 are available, use the higher of the values.)	National scale / representative data (data from UCMR has highest priority, then NCOD, then NIRS)
2a	Percentage of all Ambient/Raw/Source Monitoring Samples or Sites with Detections	National scale / representative data (NAWQA)
2b	Percentage of Ambient/Raw/Source Monitoring Samples or Sites with Detections (Note: use combined surface / ground water if available and higher of SW/GW if not)	National scale / representative data (NREC – first use National Reconnaissance data, then National Aggregate data)
3	Pesticide application data, number of states where pesticide was applied	From NCFAP
4	Environmental release data, number of states reporting releases	From TRI
5	Production volume data	From Chemical Update System/ Inventory Update Rule (CUS/IUR)

Step Two: Use scoring table to find attribute score for value identified in Step One.

For each element there is a corresponding column in the Prevalence Scoring table (see Exhibit A.5), which contains a range of data values assigned to a numeric prevalence score between 1 and 10. Once a data value has been found for a particular element, look up the value in Exhibit A.5 to determine the prevalence score. For CUS/IUR data, use the most recent year reported. For pesticides, if the compound is a degradate and does not have its own data, use the parent to score.

Exhibit A.5. Prevalence Scoring Scales

Hierarchy	1	2	3	4	5
Prevalence Score	% Finished Water PWSs with detections of contaminant All PWSs	% Ambient water sites with detections of contaminant All sites/samples	# States Reporting Pesticide in Use	# of States Reporting TRI total releases	CUS/IUR (production data) Number of pounds (by category) produced
1	<=0.10	<=0.10	--	1	<500K
2	0.11-0.16	0.11-0.16	--	2	--
3	0.17-0.25	0.17-0.25	Default for any pesticide in non-environmental use	3	>500K-1M
4	0.26-0.44	0.26-0.44	--	4	--
5	0.45-0.61	0.45-0.61	Default for any pesticide in environmental use without data	5	>1M-10M
6	0.62-1.00	0.62-1.00	<6	6	>10M-50M
7	1.01-1.30	1.01-1.30	6-10	7-10	>50M-100M
8	1.31-2.50	1.31-2.50	11-15	11-15	>100M-500M
9	2.51-10.00	2.51-10.00	16-25	16-25	>500M-1B
10	>10.00	>10.00	>25	>25	>1B

Note:
Use data in the highest category to score.
For CUS/IUR data, use the most recent year reported. Not Reported means there has been no change in production volume since the last report.
For pesticides, if the compound is a degradate and does not have its own data, use the parent to score.

A.4 Magnitude Scoring Protocol

This section describes how to assign a numerical score for the attribute Magnitude.

Step One: Identify the highest-ranked data element

When more than one data element is available for a particular contaminant, use the hierarchy below to select the preferred element. Exhibit A.6 presents the hierarchy of data elements to be used in the Magnitude scoring process. Note that the Magnitude element should be correlated with the value used to score the attribute Prevalence, except when production data are used for Prevalence and Persistence-Mobility is used for Magnitude.

Exhibit A.6. Hierarchy of Magnitude Data Elements

Rank	Magnitude Data Element	Type of Data
1	Finished Drinking Water – Median of detected concentrations from all Public Water Systems with detections (If data from both NCOD Round 1 and Round 2 are available, use the higher of the values.)	National scale finished drinking water occurrence data [data from Unregulated Contaminant Monitoring Rule (UCMR) has highest priority, then the National Contaminant Occurrence Database (NCOD), then the National Inorganics Reconnaissance Survey (NIRS)]
2a	Median of detected concentrations from all ambient / raw source monitoring sites with detections	National scale ambient monitoring data (National Water Quality Assessment Program - NAWQA)
2b	Median of detected concentrations from ambient / raw / source water samples with detections (Note: use combined surface / ground water if available and higher of SW/GW if not)	National scale / representative data (National Reconnaissance of Emerging Contaminants - NREC – first use National Reconnaissance data, then National Aggregate data)
3	Pesticide application data	From National Center for Food and Agricultural policy (NCFAP)
4	Environmental release data, total pounds or tons reported as released (TRI)	From Toxics Release Inventory (TRI)
5	Persistence – Mobility (Environmental Fate Data)	Physical chemical properties

Step Two: Use scoring table to find attribute score for value identified in Step One.

For each data element, there is a corresponding column in the Magnitude Scoring table (Exhibit A.7), which contains a range of data values assigned to a numerical magnitude score. Locate the column in the table associated with the highest-ranking data element identified in step one. Use the information in the column to determine the numerical score associated with the data value for the chemical being scored. The number corresponding to each "Score" is the maximum in that category, e.g. 0.1 µg/L for finished

water scores 4, not 5. In cases where there are no data for Scoring Magnitude in Exhibit A.7 (e.g. Prevalence is scored using Production Volume data), use the Persistence-Mobility Scoring approach to develop a Magnitude Score.

Persistence-Mobility Scoring

The approach for scoring persistence and mobility includes assigning two values, one for persistence and one for mobility, on a numeric scale of 1 through 3, representing low, medium, and high for each property as it favors the presence of the contaminant in water. Using a hierarchy of physical property data elements, each contaminant is scored for both persistence and mobility. The average of these two values is multiplied by 10/3 to obtain the persistence-mobility score. Exhibit A.8 displays the hierarchy of available properties for each data element representing either persistence or mobility.

Protocol for Persistence-Mobility Scoring

Step One: Identify and score highest-ranked data value for Persistence

When more than one data element value is available for a particular contaminant candidate, use the hierarchy below to select the preferred element. Exhibit A.6 describes the hierarchy of data elements to be used in the Persistence scoring process. When several values for a physical property are available, the highest scoring value should be used, unless that value is not representative of environmental conditions in drinking water.

Step Two: Identify and score highest-ranked data value for Mobility

The hierarchy of physical properties for scoring mobility is given in Exhibit A.6. Select the highest priority data element available for scoring. When several values for a particular physical property are available, the highest scoring value should be used for scoring, unless that value is not representative of environmental conditions in drinking water.

Step Three: Multiply the average of the persistence and mobility values by 10/3 for the magnitude score.

Exhibit A.7. Magnitude Scoring Scales

Hierarchy	1	2	3	4	5
Magnitude Scale	Finished Water Occurrence Scale	Ambient Water Occurrence Scale	Pesticide Use Scale	TRI Total Releases Scale	Persistence/ Mobility
Data Used to Score	Median of detections - all PWSs	Median of detections - all sites/samples	Number of pounds applied	Total number of pounds released	
Units	μg/L	μg/L	lbs	lbs	Used when Production data are used to score for prevalence.
Score					
1	<0.003	<0.003	<10,000	<300	
2	0.003 - 0.01	0.003 - 0.01	- -	301-1,000	

Exhibit A.7. Magnitude Scoring Scales

Hierarchy	1	2	3	4	5
Magnitude Scale	Finished Water Occurrence Scale	Ambient Water Occurrence Scale	Pesticide Use Scale	TRI Total Releases Scale	Persistence/ Mobility
Data Used to Score	Median of detections - all PWSs	Median of detections - all sites/samples	Number of pounds applied	Total number of pounds released	
3	>0.01 - 0.03	>0.01 - 0.03	10,000-30,000	1,001-3,000	See Persistence/ Mobility protocol (Exhibit A.6)
4	>0.03 - 0.1	>0.03 - 0.1	30,001-100,000	3,001-10,000	
5	>0.1 - 0.3	>0.1 - 0.3	100,001-300,000	10,001-30,000	
6	>0.3 - 1	>0.3 – 1	300,001-1M	30,001-100,000	
7	>1 - 3	>1 – 3	1M - 3M	100,001-300,000	
8	>3 - 10	>3 – 10	3M - 10M	300,001-1M	
9	>10 - 30	>10 – 30	10M - 30M	1M - 3M	
10	>30	>30	>30M	>3M	

Notes:
Use data in the highest category to score.
The number corresponding to each "Score" is the maximum in that category, e.g. 0.1 µg/L scores 4, not 5.
For pesticides, use the parent to score if the compound is a degradate and does not have its own data.

Exhibit A.8. Magnitude Scales for Environmental Fate Data

Magnitude Hierarchy 5
Mobility Scale

			Value		
		Units	**1 (Low)**	**2 (Medium)**	**3 (High)**
1	Organic Carbon Partitioning Coefficient (K_{oc})	mL/g	>1,000	100-1,000	<100
2	Log Octanol/Water Partitioning Coefficient (log K_{ow})	dimensionless	>4	1-4	<1
3	Soil/Water Distribution Coefficient (K_d)	mL/g	>10	1-10	<1
4	Henry's Law Coefficient (K_H)	atm-m^3/mol	$>10^{-3}$	10^{-7}-10^{-3}	$<10^{-7}$
5	Henry's Law Coefficient (K_H)	dimensionless	>0.042	0.042-$4.2x10^{-6}$	$<4.2x10^{-6}$
6	Solubility	mg/L	<1	1-1,000	>1,000
7	Percent in water (PBT Profiler)	dimensionless	≤ 25	>25-50	> 50

Persistence Scale

		Value		
	Units	**1 (Low)**	**2 (Medium)**	**3 (High)**

Exhibit A.8. Magnitude Scales for Environmental Fate Data

Magnitude Hierarchy 5

Mobility Scale			**Value**		
		Units	**1 (Low)**	**2 (Medium)**	**3 (High)**
1	Half Life ($t_{1/2}$)	time	days, days-weeks	weeks, weeks-months	months, recalcitrant
2	Measured Degradation Rate[1]	time	days, days-weeks (BF, BFA)[2]	weeks, weeks-months (BS, BSA)	months, recalcitrant (BST)
3	Modeled Degradation Rate (PBT Profiler)	time	days, days-weeks	weeks, weeks-months	months, recalcitrant

[1] When two results are found for a measured degradation rate, the data are "averaged" and then a value determined.

[2] BF = Biodegrades Fast, BFA = Biodegrades Fast with Acclimation, BS = Biodegrades Slow, BST = Biodegrades Sometimes.

Appendix B. Example Blinded Information Sheets from the TDS Exercises

Contaminant 3

Contaminant Name:											
Background:	It is a volatile organic chemical. It is used as a wetting and dispersing agent in textile processing, dye-baths, stain and printing compositions; used in cleaning and detergent preparations, adhesives, cosmetics, deodorants, fumigants, emulsions and polishing compositions. Used in lacquers, paints, varnishes, paint and varnish removers. Degreasing agent. It is on the TSCA list. The reportable released quantity of this substance under CERCLA is 1 lb. It is also subject to RCRA waste management requirements, and is listed as a hazardous air pollutant by EPA. Several states have drinking water guidelines for this chemical (CA, FL, MA, ME, NC). Its one-day Health Advisory Level (HAL) is 4,000 µg/L, its 10-day HAL is 400 µg/L, and its 10^-4 cancer risk HAL is 300 µg/L. This is an HPV chemical. It is also on the CCL. (HSDB, 2005; EPAHA, 2004)										
HEALTH EFFECTS DATA											
Data Element	**Value**	**Units**	**Source**			**Notes**					
Reference Dose	N/A										
Carcinogen classification (EPA)	B2 (probable human carcinogen)		IRIS			9/1/1990					
Slope Factor	0.011	1/(mg/kg-d)	IRIS			9/1/1990					
Carcinogen Classification (IARC)	2B (possible)		IARC								
Non EPA Derived Dose[1]	0.1	mg/kg-d	ATSDR MRL			Chronic oral					
Critical Effect	Hepatic effects					UF=100					
File/Issue Date	10/1/2004										
Lowest Oral Chronic LOAEL[1]	N/A										
Lowest Oral LD50[1]	N/A										
Is contaminant on list of carcinogens?	Y	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity			1/1/1988					

Contaminant 3

Is the contaminant on a list of reproductive toxins?	N	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity								
Risk assessment ongoing?	Y	Y/N									
Health Reference Level (HRL)[2]	700	µg/L	Based on MRL								
Health Reference Level (HRL)[2] cancer	3.18	µg/L									
Health Reference Level (HRL) cancer	300	µg/L	10^{-4} cancer risk Health Advisory (EPAHA, 1987)								
Notes											
[1] Non-EPA toxicology data will be sought if no EPA Reference Dose or carcinogen information available; may require multiple entries; chronic studies will be prioritized over short term studies.											
[2] Health Reference Level calculated by conversion of RfD or other dose to units of µg/L, assuming 2 liters per day of water consumed by a 70 Kg adult, and a default Relative Source Contribution of 20%. For carcinogens, the concentration at the 10^{-6} cancer risk level will be converted to units of µg/L and will also be listed.											
OCCURRENCE DATA											

Water Occurrence Data	**# PWSs/Sites sampled**	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Median of Detects (µg/L)**	**99% of Detects (µg/L)**	**Source**	**Notes**		
Finished Water Occurrence - total	No Data	No Data	No Data	No Data	No Data	No Data	No Data				
	# PWSs/Sites sampled	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Median of Detects (µg/L)**	**Mean of Detects (µg/L)**	**90% of Detects (µg/L)**	**95% of Detects (µg/L)**	**99% of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Source**
Source Water-Total	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	
Production/Release	**Value**	**Units**	**Source**			**Notes**					
Production data	>1M - 10M	lbs/yr	CUS-IUR (2002)								
Pesticide Application - total	N/A	lbs/yr									
Pesticide Application - total (# States)	N/A	# States									
Release - total	1,146,641	lbs/yr	TRI								

Contaminant 3

Release - total (# States)	22	# States	TRI								
Release - to Surface Water	75,119	lbs/yr	TRI								
Release - to SW (# States)	9	# States	TRI								
Environmental Fate Parameters	**Value**	**Units**	**Source**			**Notes**					
$T_{1/2}$, Half life	No Data	length of time									
K_{OC}, Organic Carbon Partition Coefficient	1	L/kg	RAISCF								
K_{OW}, Octanol Water Partition Coefficient	Log -0.27	unitless	RAISCF								
HLC, Henry's Law Constant	0.000196	unitless	RAISCF								
Water Solubility	1,000,000	mg/L	RAISCF								
Kd, Distribution Coefficient	N/A	source specific									
No Data = No data found for this contaminant; N/A = Not applicable to contaminant											

Contaminant Name:											
Background:	This is a volatile organic chemical. It is used as a food additive, organic intermediate, solvent, and in cosmetic formulations. It is also used as a solvent or solubilizer in the paint and printing ink sector, as components in textile auxiliaries and pesticides, for hormone extraction, and in the surfactant field as foam boosters or antifrothing agents. Per the FDA, this food additive is permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant. (HSDB, 2005)										
HEALTH EFFECTS DATA											
Data Element	**Value**	**Units**	**Source**			**Notes**					
Reference Dose	N/A										
Carcinogen classification (EPA)	N/A										
Slope Factor	N/A										
Carcinogen Classification (IARC)	N/A										
Non EPA Derived Dose[1]	N/A										
Lowest Oral Chronic LOAEL[1]	N/A										
Lowest Oral LD50[1]	500	mg/kg	RTECS								
Is contaminant on list of carcinogens?	N	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity								

Contaminant 4

Is the contaminant on a list of reproductive toxins?	N	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity								
Risk assessment ongoing?	N	Y/N									
Health Reference Level (HRL)[2]	N/A	µg/L									
Health Reference Level (HRL)[2] cancer	N/A	µg/L									
Notes											
[1] Non-EPA toxicology data will be sought if no EPA Reference Dose or carcinogen information available; may require multiple entries; chronic studies will be prioritized over short term studies.											
[2] Health Reference Level calculated by conversion of RfD or other dose to units of µg/L, assuming 2 liters per day of water consumed by a 70 Kg adult, and a default Relative Source Contribution of 20%. For carcinogens, the concentration at the 10^{-6} cancer risk level will be converted to units of µg/L and will also be listed.											
OCCURRENCE DATA											

Water Occurrence Data	**# PWSs/Sites sampled**	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Median of Detects (µg/L)**	**99% of Detects (µg/L)**	**Source**	**Notes**		
Finished Water Occurrence - total	No Data	No Data	No Data	No Data	No Data	No Data	No Data				
	# PWSs/Sites sampled	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Median of Detects (µg/L)**	**Mean of Detects (µg/L)**	**90% of Detects (µg/L)**	**95% of Detects (µg/L)**	**99% of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Source**
Source Water-Total	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	

Production/Release	**Value**	**Units**	**Source**			**Notes**					
Production data	>500K - 1M	lbs/yr	CUS-IUR (2002)								
Pesticide Application - total	N/A	lbs/yr									
Pesticide Application - total (# States)	N/A	# States									
Release - total	No Data	lbs/yr									

Contaminant 4

Release - total (# States)	No Data	# States									
Release - to Surface Water	No Data	lbs/yr									
Release - to SW (# States)	No Data	# States									
Environmental Fate Parameters	**Value**	**Units**	**Source**			**Notes**					
$T_{1/2}$, Half life	No Data	length of time									
K_{OC}, Organic Carbon Partition Coefficient	15	L/kg	HSDB								
K_{OW}, Octanol Water Partition Coefficient	Log 2.62	unitless	HSDB								
HLC, Henry's Law Constant	1.88E-05	atm-cu m/mol	HSDB								
Water Solubility	1000	mg/L	HSDB								
Kd, Distribution Coefficient	N/A	source specific									
No Data = No data found for this contaminant; N/A = Not applicable to contaminant											

Contaminant 5

Contaminant Name:											
Background:	This is a volatile organic chemical registered for use in the U.S. Nematicide. Seventh most commonly used pesticide in U.S. agricultural crop production. Used in organic synthesis and in manufacture of pesticides. Pre-plant soil fumigant. It is listed on FIFRA and TSCA. The reportable release quantity under CERCLA is 100 lbs. It is subject to RCRA waste management requirements. It is listed as a hazardous air pollutant and as a hazardous substance by the Federal Water Pollution Control Act and the Clean Water Act. It has a state drinking water standard in CA. It has a state drinking water guideline in several states (FL, MA, ME, MN, WI). It has a DWEL of 1,000 µg/L, and its one-day and ten-day Health Advisory Levels (HALs) are 30 µg/L. This is an HPV chemical. (HSDB, 2005; EPAHA, 2004)										
HEALTH EFFECTS DATA											
Data Element	**Value**	**Units**	**Source**			**Notes**					
Reference Dose	0.03	mg/kg-d	IRIS			Basis = BMDL(10) 3.4 mg/kg-d Rat, UF=100, MF=1					
Critical Effect	Chronic irritation					Confidence: Study: High; Database: High; RfD: High					
File/Issue Date	5/25/2000										
Reference Dose	0.025	mg/kg-d	OPP			Basis = NOEL 2.5 mg/kg-d Rat, UF=100, MF=1					
Critical Effect	decrease in body weight gain and an increase in the incidence of basal cell hyperplasia of the nonglandular mucosa of the stomach										
File/Issue Date	1998										
Carcinogen classification (EPA)	B2; inadequate in humans, sufficient in animals			IRIS		5/25/2000					
Slope Factor	0.1	1/(mg/kg-d)	IRIS								
Carcinogen Classification (IARC)	2B (possible)		IARC								
Non EPA Derived Dose[1]	N/A										
Lowest Oral Chronic LOAEL[1]	N/A										
Lowest Oral LD50[1]	N/A										

Contaminant 5

Is contaminant on list of carcinogens?	Y	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity			1/1/1989					
Is the contaminant on a list of reproductive toxins?	N	Y/N	Cal EPA Chemicals Known to the State to Cause Cancer or Reproductive Toxicity								
Risk assessment ongoing?	N	Y/N									
Health Reference Level (HRL)[2]	210	µg/L	Based on IRIS RfD								
Health Reference Level (HRL)[2] cancer	0.35	µg/L	Based on IRIS slope factor								
Health Reference Level (HRL) cancer	40	µg/L	10^{-4} cancer risk Health Advisory (EPAHA, 1988)								
Notes											
[1] Non-EPA toxicology data will be sought if no EPA Reference Dose or carcinogen information available; may require multiple entries; chronic studies will be prioritized over short term studies.											
[2] Health Reference Level calculated by conversion of RfD or other dose to units of µg/L, assuming 2 liters per day of water consumed by a 70 Kg adult, and a default Relative Source Contribution of 20%. For carcinogens, the concentration at the 10^{-6} cancer risk level will be converted to units of µg/L and will also be listed.											
OCCURRENCE DATA											

Water Occurrence Data	**# PWSs/Sites sampled**	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Median of Detects (µg/L)**	**99% of Detects (µg/L)**	**Source**	**Notes**
Finished Water Occurrence - total	9,164	15	0.16%	0.5	2	1	2	NCOD Round 1	
Finished Water Occurrence - SW	898	5	0.56%	1	2	1.25	2	NCOD Round 1	
Finished Water Occurrence - GW	8,303	10	0.12%	0.5	1.6	0.5	1.6	NCOD Round 1	

Contaminant 5

Finished Water Occurrence - total	16,787	58	0.35%	0.2	39	0.5	39	NCOD Round 2			
Finished Water Occurrence - SW	1,609	10	0.62%	0.2	1.6	0.5	1.6	NCOD Round 2			
Finished Water Occurrence - GW	15,178	48	0.32%	0.2	39	0.5	39	NCOD Round 2			
	# PWSs/Sites sampled	**# with Detects**	**% Detects**	**Minimum of Detects (µg/L)**	**Median of Detects (µg/L)**	**Mean of Detects (µg/L)**	**90% of Detects (µg/L)**	**95% of Detects (µg/L)**	**99% of Detects (µg/L)**	**Maximum of Detects (µg/L)**	**Source**
Source Water-Total	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	
Production/Release	**Value**	**Units**	**Source**			**Notes**					
Production data	>1M - 10M	lbs/yr	CUS-IUR (2002)								
Pesticide Application - total	34,717,237	lbs/yr	NCFAP								
Pesticide Application - total (# States)	20	# States	NCFAP								
Release - total	10,532	lbs/yr	TRI								
Release - total (# States)	8	# States	TRI								
Release - to Surface Water	85	lbs/yr	TRI								
Release - to SW (# States)	3	# States	TRI								
Environmental Fate Parameters	**Value**	**Units**	**Source**			**Notes**					
$T_{1/2}$, Half life	No Data	length of time									
K_{OC}, Organic Carbon Partition Coefficient	81	L/kg	RAISCF								

K_{OW}, Octanol Water Partition Coefficient	Log 2.03	unitless	RAISCF								
HLC, Henry's Law Constant	0.145	unitless	RAISCF								
Water Solubility	2,800	mg/L	RAISCF								
Kd, Distribution Coefficient	N/A	source specific									
No Data = No data found for this contaminant; N/A = Not applicable to contaminant											

APPENDIX C. Summary of EPA Team TDS Decisions

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
1	2	7	1	1	1.00	1	NL
2	5	8	10	8	3.67	4	L
3	5	7	1	1	1.17	1	NL
4	4	3	7	6	1.83	2	NL?
5	6	8	6	7	3.50	4	L
6	3	3	10	10	2.17	2	NL?
7	4	9	10	10	3.17	3	L?
8	5	8	8	7	3.67	4	L
9	4	5	10	10	3.17	3	L?
10	5	6	1	6	1.67	2	NL?
11	6	9	10	7	3.67	4	L
12	4	3	10	9	2.50	3	L?
13	3	3	10	10	2.00	2	NL?
14	6	8	10	7	3.83	4	L
15	8	7	9	8	4.00	4	L
16	4	5	2	6	1.67	2	NL?
17	6	5	6	7	2.83	3	L?
18	7	3	9	8	3.33	3	L?
19	5	6	9	8	3.17	3	L?
20	4	5	2	6	1.50	2	NL?
21	3	6	9	10	3.17	3	L?
22	4	3	6	6	1.50	2	NL?
23	5	5	10	5	2.67	3	L?
24	5	7	1	1	1.17	1	NL
25	5	3	10	9	3.00	3	L?
26	3	3	9	3	1.50	2	NL?
27	7	6	4	5	2.83	3	L?
28	4	3	10	9	2.50	3	L?
29	4	5	5	8	2.33	2	NL?
30	4	3	9	3	1.50	2	NL?
31	6	5	1	10	2.00	2	NL?
32	4	3	10	10	2.50	3	L?
33	8	8	1	6	2.83	3	L?
34	5	8	9	7	3.67	4	L
35	5	4	10	8	2.83	3	L?
36	7	3	1	1	1.17	1	NL
37	7	3	1	1	1.00	1	NL
38	7	8	4	4	3.00	3	L?
39	4	3	10	10	2.50	3	L?

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
40	6	3	9	2	1.83	2	NL?
41	5	3	1	6	1.50	2	NL?
42	5	3	7	6	2.00	2	NL?
43	4	4	10	10	2.83	3	L?
44	3	1	3	1	1.00	1	NL
45	2	3	7	8	1.33	1	NL
46	5	8	1	5	2.17	2	NL?
47	4	3	9	7	2.17	2	NL?
48	4	3	8	8	2.33	2	NL?
49	4	8	9	9	3.67	4	L
50	2	3	10	10	1.83	2	NL?
51	5	8	4	6	2.83	3	L?
52	5	8	1	1	1.17	1	NL
53	6	8	1	1	1.17	1	NL
54	5	5	10	10	3.50	4	L
55	6	9	3	7	3.00	3	L?
56	3	3	10	10	2.00	2	NL?
57	6	6	9	6	3.33	3	L?
58	5	8	4	4	2.67	3	L?
59	8	8	3	6	3.33	3	L?
60	5	3	4	8	2.00	2	NL?
61	5	7	9	6	3.50	4	L
62	7	6	1	1	1.33	1	NL
64	4	3	9	7	2.33	2	NL?
65	4	6	10	10	3.33	3	L?
66	7	8	10	8	4.00	4	L
67	5	6	2	7	2.17	2	NL?
68	7	8	1	1	1.67	2	NL?
69	7	8	7	4	3.33	3	L?
70	4	6	1	1	1.00	1	NL
71	5	5	1	1	1.00	1	NL
72	7	8	3	6	3.33	3	L?
73	8	8	7	6	3.83	4	L
74	6	8	1	1	1.17	1	NL
75	3	3	10	8	1.83	2	NL?
76	10	6	9	8	4.00	4	L
77	4	7	7	5	2.67	3	L?
78	5	3	2	3	1.17	1	NL
79	4	3	6	7	1.83	2	NL?
80	7	3	10	6	2.83	3	L?
81	4	3	10	8	2.33	2	NL?

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
82	3	6	10	10	2.83	3	L?
83	3	8	4	7	2.50	3	L?
84	4	8	10	6	3.33	3	L?
85	3	3	10	8	1.80	2	NL?
86	7	6	5	7	3.20	3	L?
87	4	6	3	5	1.80	2	NL?
88	6	8	5	8	3.60	4	L
89	6	6	6	8	3.00	3	L?
90	4	6	6	7	2.40	2	NL?
91	5	8	1	5	2.20	2	NL?
92	4	6	1	7	1.80	2	NL?
93	3	3	5	7	1.20	1	NL
94	4	6	3	5	1.40	1	NL
95	6	3	6	7	2.40	2	NL?
96	4	4	10	7	2.40	2	NL?
97	6	5	8	7	3.20	3	L?
98	4	8	5	10	3.60	4	L
99	7	9	5	8	3.80	4	L
100	3	8	1	7	1.80	2	NL?
101	5	6	3	7	2.60	3	L?
102	4	8	8	7	3.00	3	L?
Synthetic Chemicals:							
63	4	1	7	7	1.50	2	NL?
149	3	2	2	2	1.00	1	NL
150	5	3	1	2	1.00	1	NL
151	6	1	2	1	1.00	1	NL
152	2	8	1	1	1.00	1	NL
153	6	9	1	4	2.33	2	NL?
154	8	8	8	2	3.50	4	L
155	2	2	10	9	2.00	2	NL?
156	4	1	8	1	1.00	1	NL
157	7	3	8	3	2.00	2	NL?
158	4	8	8	1	2.33	2	NL?
159	10	8	8	1	3.50	4	L
160	1	3	5	9	1.33	1	NL
161	9	1	1	7	1.67	2	NL?
162	1	1	1	1	1.00	1	NL
163	2	6	1	9	1.83	2	NL?
164	7	8	4	7	3.67	4	L
165	4	5	10	9	3.17	3	L?

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
166	7	3	10	10	3.67	4	L
167	2	6	7	7	2.17	2	NL?
168	6	6	7	5	2.67	3	L?
169	10	9	10	7	4.00	4	L
170	5	1	5	3	1.00	1	NL
171	9	3	3	3	2.00	2	NL?
172	3	6	1	3	1.00	1	NL
173	8	7	1	2	2.33	2	NL?
174	10	5	1	1	2.00	2	NL?
175	8	8	8	8	4.00	4	L
176	1	5	10	3	1.33	1	NL
177	10	4	8	5	3.33	3	L?
178	3	8	10	1	1.83	2	NL?
179	10	8	9	4	3.83	4	L
180	5	4	3	8	2.50	3	L?
181	2	2	10	7	1.17	1	NL
182	8	5	3	8	3.33	3	L?
183	1	8	5	10	2.83	3	L?
184	6	8	2	6	3.00	3	L?
185	1	2	9	8	1.33	1	NL
186	6	5	6	6	2.83	3	L?
187	8	8	8	6	3.83	4	L
188	1	8	7	7	2.17	2	NL?
189	9	8	7	10	4.00	4	L
190	5	4	3	3	1.17	1	NL
191	10	4	5	3	2.67	3	L?
192	5	6	3	5	2.17	2	NL?
193	9	8	9	9	4.00	4	L
194	6	6	1	1	1.17	1	NL
195	2	1	8	3	1.17	1	NL
196	6	2	8	2	1.50	2	NL?
197	3	7	6	3	2.17	2	NL?
198	6	8	8	1	2.83	3	L?
199	9	8	2	3	3.17	3	L?
200	3	1	1	6	1.17	1	NL
201	8	2	2	7	2.33	2	NL?
202	4	9	5	7	3.33	3	L?
203	8	8	1	7	3.50	4	L
204	3	5	6	8	2.33	2	NL?
205	9	8	9	4	3.67	4	L
206	10	2	1	1	1.50	2	NL?

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
207	8	4	6	9	3.33	3	L?
208	4	8	8	7	3.67	4	L
209	7	6	9	8	3.83	4	L
210	4	4	1	4	1.00	1	NL
211	9	3	4	3	2.33	2	NL?
212	7	7	7	7	3.50	4	L
213	4	7	3	5	2.17	2	NL?
214	7	8	1	4	2.67	3	L?
215	1	4	10	2	1.33	1	NL
216	6	3	10	5	2.50	3	L?
217	2	8	9	3	2.17	2	NL?
218	2	3	10	5	1.17	1	NL
219	8	8	6	5	3.67	4	L
220	5	3	3	10	2.50	3	L?
221	10	3	2	6	2.83	3	L?
222	5	8	2	6	2.67	3	L?
223	8	7	2	7	3.33	3	L?
224	7	7	9	4	3.67	4	L
225	2	4	6	9	2.33	2	NL?
226	8	3	10	6	3.50	4	L
227	1	8	7	8	2.33	2	NL?
228	10	8	6	8	3.83	4	L
229	4	4	4	2	1.00	1	NL
230	10	8	2	9	3.67	4	L
231	6	4	5	3	2.00	2	NL?
232	1	6	5	1	1.00	1	NL
233	7	6	4	2	2.00	2	NL?
234	2	3	10	4	1.00	1	NL
235	8	2	7	2	1.50	2	NL?
236	6	9	6	6	3.67	4	L
237	2	8	7	4	2.00	2	NL?
238	8	8	8	4	3.83	4	L
239	5	4	1	6	2.33	2	NL?
240	8	1	1	7	1.67	2	NL?
241	4	7	4	7	2.83	3	L?
242	10	8	10	3	3.83	4	L
243	9	7	4	6	3.83	4	L
244	4	1	8	9	2.00	2	NL?
245	7	2	10	6	2.67	3	L?
246	3	8	10	9	3.67	4	L
247	9	8	7	8	4.00	4	L

Chemical ID	INPUT ATTRIBUTE SCORES				Team Consensus Blinded Decisions		
Blinded Chemical Algorithm Number	Potency	Severity	Prevalence	Magnitude	List=4 Mean	Integer Score	L/NL
Real Chemicals:							
248	1	1	10	5	1.17	1	NL

APPENDIX D. SOFTWARE SOURCES

Artificial Neural Networks – ANN methods packaged in R software libraries "MASS" and "nnet" are available at no charge from the website http://www.r-project.org, under the Free Software Foundation's GNU General Public License.

Univariate Decision Tree – CART – methods packaged in the R software library "rpart" are available at no charge from the website http://www.r-project.org, under the Free Software Foundation's GNU General Public License.

Multivariate Decision Tree – QUEST software is available at no charge from the website http://www.stat.wisc.edu/~loh/quest.html

Linear Modeling - Likelihood function was maximized using MathCAD's built-in Maximize function (www.mathsoft.com).

Multivariate Adaptive Regression Splines – MARS methods packaged in the R software library "polspline" are available at no charge from the website http://www.r-project.org, under the Free Software Foundation's GNU General Public License.

APPENDIX E. SOLUTIONS

Artificial Neural Network – The software used does not reveal its decision rule. Instead, it provides classifications for contaminants that have been scored for the four attributes. When given a complete set of all possible combinations of integer attribute scores, the software provides classifications. Although not expressed mathematically, this complete description of the decision rule can be seen in Exhibit 4-4.

Example: Contaminant with scores (3, 4, 5, 6). Exhibit 4-4 shows this as a dark blue point. **Not List**.

Simple Linear Model – The maximum likelihood linear model is shown below. Y[i] is the estimated team-average classification and Pot[i], Sev[i], Prev[i], Mag[i] are the attribute scores for contaminant i. If Y[i] is less than 1.5, then the classification is Not List. Similarly, if Y[i] is at least 3.5, then the classification is List.

$$Y[i] = -1.671 + 0.241 * Pot[i] + 0.217 * Sev[i] + 0.116 * Prev[i] + 0.170 * Mag[i]$$

Example: Contaminant with scores (3, 4, 5, 6).

$Y = -1.671 + 0.241 * 3 + 0.217 * 4 + 0.116 * 5 + 0.170 * 6 = 1.520$ → **Not List**

Multivariate Tree (QUEST) – The solution involves a number of intermediate nodes and terminal nodes arranged as shown in Exhibit 4.1.1. When a contaminant encounters an intermediate node, a weighted sum of attribute scores is compared to a threshold value. The direction the contaminant moves from the node depends on whether the threshold is exceeded. Below, vector notation is used below to simplify the description. Letting X[i] be a column vector of attribute scores, (Pot[i], Sev[i], Prev[i], Mag[i]), then $B1^T*X[i]$ is the vector product of B1 (a column vector of weights) and X[i], which, in turn, is compared with the threshold. When the contaminant encounters a terminal node (Node 6, 10, 11, 16, 17, 29, 30, or 31), a classification is assigned.

Node 1: If **B1***X[i] ≤ 0.3023, then Node 2, otherwise Node 3.
- Node 2: If **B2***X[i] ≤ 0.3844, then Node 4, otherwise Node 5.
  - Node 4: If **B4***X[i] ≤ 0.6460, then Node 6, otherwise Node 7.
    - Node 6: **Not List**
    - Node 7: If **B7***X[i] ≤ 3.336, then Node 10, otherwise Node 11.
      - Node 10: **Not List**
      - Node 11: **Not List?**
  - Node 5: If **B5***X[i] ≤ 1.213, then Node 16, otherwise Node 17.
    - Node 16: **Not List?**
    - Node 17: **List?**
- Node 3: If **B3***X[i] ≤ 1.181, then Node 28, otherwise Node 29
  - Node 28: If **B28***X[i] ≤ 6.460, then Node 30, otherwise Node 31.
    - Node 30: **List?**
    - Node 31: **List**
  - Node 29: **List**

Exhibit A.1 – Tree Produced by QUEST (heavy arrows show path of contaminant with attribute scores 3, 4, 5, 6)

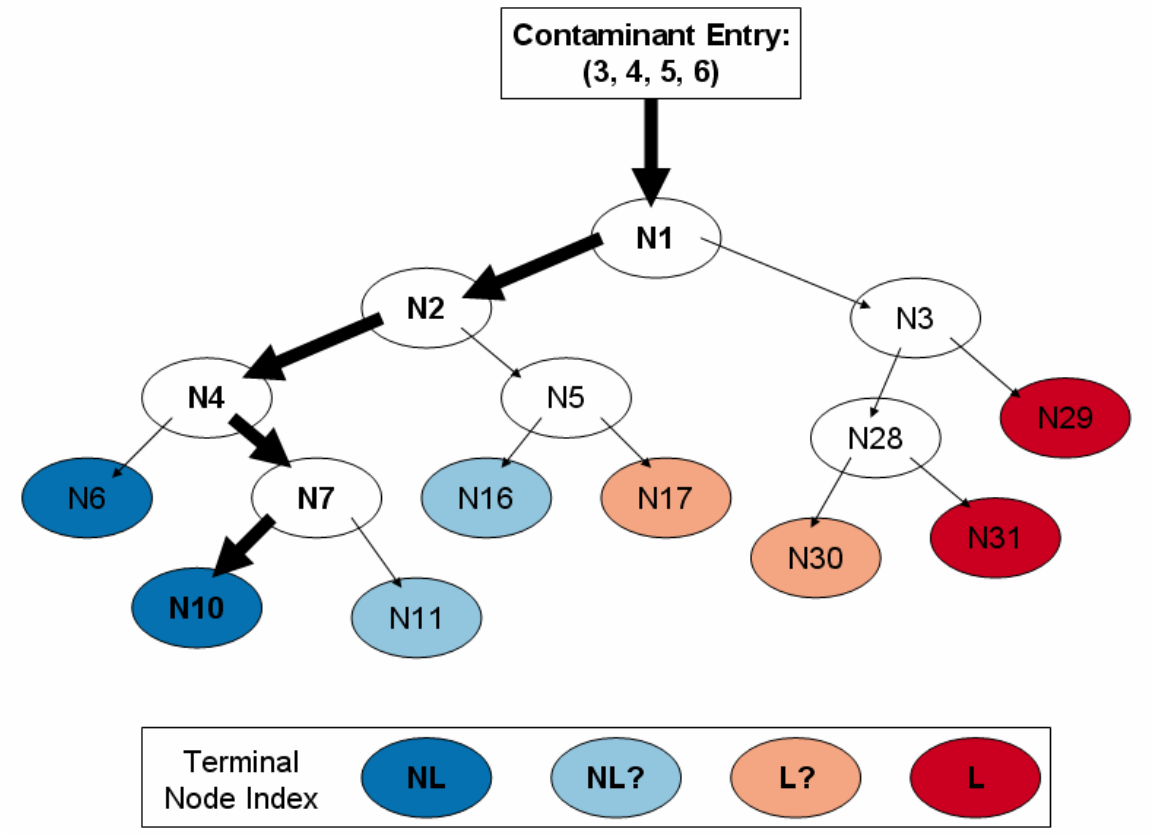

Exhibit A.2 - The column vectors of weights:

B1	B2	B3	B4	B5	B7	B28
0.01631	0.03008	0.05223	0.06890	0.07779	0.3531	0.2966
0.01315	0.02075	0.06855	0.01756	0.06447	0.1136	0.3174
0.007523	0.01214	0.03516	0.01753	0.03300	0.07560	0.1995
0.01034	0.02043	0.01807	0.05501	0.04850	0.2144	0.1952

Example: Contaminant with scores X = (3, 4, 5, 6)

Node 1: $B1^{T}*X = 0.01631*3 + 0.01315*4 + 0.007523*5 + 0.01034*6 = 0.2012$
This is less than 0.3023, so go to Node 2.

Node 2: $B2^{T}*X = 0.03008*3 + 0.02075*4 + 0.01214*5 + 0.02043*6 = 0.3565$
This is less than 0.3844, so go to Node 4.

Node 4: $B4^{T}*X = 0.06890*3 + 0.01756*4 + 0.01753*5 + 0.05501*6 = 0.6947$
This exceeds 0.6460, so go to Node 7.

Node 7: $B7^T*X = 0.3531*3 + 0.1136*4 + 0.07560*5 + 0.2144*6 = 3.1781$
This is less than 3.336, so go to Node 10.

Node 10: **Not List**

[1]If Y[i] is between 1.5 and 2.5, the classification is NL?; and if Y[i] is between 2.5 and 3.5, the classification is L?

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

Set 1 Summary					Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
51285	2,4-Dinitrophenol	**NL**	18	100	+/-0	1.00	NL	65%	35%	0%	2.647	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
60571	Dieldrin	**L? - L**	18	83	+7	3.66	L	41%	47%	12%	2.294	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
62737	Dichlorvos	**NL - NL?**	16	88	-1	1.63	NL?	33%	53%	13%	2.200	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Percentage of Samples (Detects), Surface Water, Ambient	NREC
63252	Carbaryl	**NL?**	16	69	+/-0	2.00	NL?	33%	47%	20%	2.133	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
67641	Acetone	**L?**	18	78	-2	2.75	L?	40%	60%	0%	2.400	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
67721	Hexachloroethane	**NL**	17	100	+1	1.06	NL	44%	56%	0%	2.438	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
72559	p,p'-DDE	**NL - NL?**	16	88	+1	1.61	NL?	40%	53%	7%	2.333	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
74839	Methyl bromide Bromomethane	**L?**	17	82	+3	3.11	L?	47%	47%	7%	2.400	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
74873	Chloromethane (Methyl chloride)	**L?**	16	81	+/-0	2.88	L?	50%	50%	0%	2.500	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
74953	Dibromomethane	**NL?**	14	71	-1	1.92	NL?	36%	57%	7%	2.286	Reference Dose (RfD)	RAISHE	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
74975	Halon 1011 (bromochloromethane)	**NL?**	13	62	-2	1.83	NL?	40%	60%	0%	2.400	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
75150	Carbon disulfide	**NL? - L?**	15	53	-2	2.21	NL?	29%	64%	7%	2.214	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
75343	1,1-Dichloroethane	**L?**	12	67	+1	3.00	L?	18%	64%	18%	2.000	Slope Factor (Oral)	OEHHA	CAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
75694	CFC-11. Trichlorofluoromethane	**L? - L**	13	69	+1	3.38	L?	42%	50%	8%	2.333	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
75718	CFC-12. Dichlorofluoromethane	**NL?**	13	77	-4	1.71	NL?	50%	42%	8%	2.417	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

Set 1 Summary					Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
79345	1,1,2,2-Tetrachloroethane	**NL?**	14	64	+1	2.04	NL?	36%	55%	9%	2.273	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
80626	Methyl methacrylate	**NL**	13	100	+/-0	1.00	NL	58%	42%	0%	2.583	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
86500	Azinphos-methyl	**NL?**	12	100	+1	2.15	NL?	27%	64%	9%	2.182	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
87616	1,2,3-Trichlorobenzene	**NL - NL?**	13	77	-3	1.47	NL	42%	42%	17%	2.250	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
87683	Hexachlorobutadiene	**L?**	13	77	-2	2.75	L?	46%	46%	8%	2.385	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
88062	2,4,6-Trichlorophenol	**NL**	13	92	+1	1.08	NL	42%	50%	8%	2.333	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
91203	Naphthalene	**NL?**	13	85	-1	1.93	NL?	67%	33%	0%	2.667	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
94746	MCPA	**NL? - L?**	14	71	-1	2.38	NL?	33%	42%	25%	2.083	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
95498	o-Chlorotoluene	**NL?**	13	77	-4	1.71	NL?	58%	42%	0%	2.583	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
95636	1,2,4-Trimethylbenzene	**NL?**	13	69	-1	1.92	NL?	33%	33%	33%	2.000	Reference Dose (RfD)	RAISHE	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

	Set 2 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
2212671	Molinate	**L?**	19	84	-1	3	L?	32%	58%	11%	2.211	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
2312358	Propargite	**L?**	18	72	-5	3	L?	24%	59%	18%	2.059	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
5989275	(D)-Limonene	**NL?**	17	82	-4	2	NL?	24%	59%	18%	2.059	No Observed Effect Level (NOEL)	NTP	NCAR	Percentage of Samples (Detects), Surface Water, Ambient	NREC
7439987	Molybdenum	**L? - L**	18	78	+/-0	3	L?	50%	39%	11%	2.389	UL	IOM	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440020	Nickel	**L?**	18	89	-2	3	L?	28%	67%	6%	2.222	Reference Dose (RfD)	IRIS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440097	Potassium	**L?**	18	44	-9	2	NL?	24%	24%	53%	1.706	Lowest Observed Adverse Effect Level (LOAEL)	NAS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440213	Silicon	**L**	18	61	-4	3	L?	17%	33%	50%	1.667	Lethal Dose 50 (LD50)	RTECS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440235	Sodium	**L?**	19	68	-3	3	L?	26%	37%	37%	1.895	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440246	Strontium	**L?**	19	74	+/-0	3	L?	26%	47%	26%	2.000	Reference Dose (RfD)	IRIS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440428	Boron	**L?**	18	61	+3	3	L?	24%	53%	24%	2.000	Reference Dose (RfD)	IRIS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440484	Cobalt	**NL? - L?**	17	71	-1	2	NL?	24%	53%	24%	2.000	MRL-Int	ATSDR	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7440564	Germanium	**L?**	18	61	-2	3	L?	18%	24%	59%	1.588	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

	Set 2 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
7440622	Vanadium	**L? - L**	18	78	-4	3	L?	18%	59%	24%	1.941	MRL-Int	ATSDR	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
7664417	Ammonia	**NL?**	17	82	-4	2	NL?	24%	65%	12%	2.118	Reference Dose (RfD)	RAISHE	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
7723140	White Phosphorus	**L**	19	100	-1	4	L	63%	32%	5%	2.579	Reference Dose (RfD)	IRIS	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
13071799	Terbufos	**NL**	17	82	+3	1	NL	63%	31%	6%	2.563	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
13194484	Ethoprop	**NL?**	16	81	+2	2	NL?	33%	39%	28%	2.056	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
13494809	Tellurium	**NL? - L?**	16	56	+2	2	NL?	18%	18%	65%	1.529	NOAEL	Journal	NCAR	Percentage of Samples (Detects), All Water, Finished	NIRS
14797730	Perchlorate	**NL? - L?**	16	50	+6	3	L?	33%	47%	20%	2.133	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
16655826	3-Hydroxycarbofuran	**L?**	18	83	+2	3	L?	29%	53%	18%	2.118	RfD	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
16752775	Methomyl	**NL?**	16	56	-1	2	NL?	27%	67%	7%	2.200	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
21087649	Metribuzin	**NL - NL?**	16	69	+/-0	2	NL?	50%	31%	19%	2.313	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
21725462	Cyanazine	**NL?**	17	65	+/-0	2	NL?	31%	63%	6%	2.250	Reference Dose (RfD)	EPAHA	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
25013165	Butylated hydroxyanisole	**NL?**	15	73	+/-0	2	NL?	13%	40%	47%	1.667	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of Samples (Detects), Surface Water, Ambient	NREC
25057890	Bentazon	**NL?**	15	53	+1	2	NL?	36%	57%	7%	2.286	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
27314132	Norflurazon	**NL?**	14	79	+2	2	NL?	31%	46%	23%	2.077	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA

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	Set 2 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
34014181	Tebuthiuron	**NL - NL?**	15	73	-4	1	NL	53%	33%	13%	2.400	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
34256821	Acetochlor	**NL**	16	69	+4	1	NL	67%	20%	13%	2.533	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
51218452	Metolachlor	**NL?**	13	69	-3	2	NL?	38%	54%	8%	2.308	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

	Set 3 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
96184	1,2,3-Trichloropropane	**NL?**	16	75	+1	2.12	NL?	44%	31%	25%	2.188	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
96333	Methyl acrylate	**NL**	15	93	+1	1.07	NL	40%	53%	7%	2.333	Reference Dose (RfD)	RAISHE	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
98066	tert-Butylbenzene	**NL?**	16	75	-1	1.97	NL?	19%	69%	13%	2.063	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
98953	Nitrobenzene	**NL?-L?**	16	44	+5	2.75	L?	31%	38%	31%	2.000	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
103651	n-Propylbenzene	**NL?**	16	94	+1	2.03	NL?	31%	50%	19%	2.125	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
106434	p-Chlorotoluene	**NL?**	15	87	-1	1.94	NL?	31%	56%	13%	2.188	Reference Dose (RfD)	EPAHA / IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
107028	Acrolein	**L?-L**	16	69	+1	3.53	L	25%	63%	13%	2.125	Reference Dose (RfD)	RAISHE	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
107131	Acrylonitrile	**NL?-NL**	15	73	+3	1.78	NL?	20%	73%	7%	2.133	Lifetime Cancer Risk (10^-4)	EPAHA	CAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
108054	Vinyl acetate	**NL**	15	100	+/- 0	1.00	NL	40%	47%	13%	2.267	Reference Dose (RfD)	RAISHE	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
108861	Bromobenzene	**NL?**	16	69	+3	2.09	NL?	27%	53%	20%	2.067	Reference Dose (RfD)	RAISHE	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
109999	Tetrahydrofuran	**L?**	16	75	-1	2.93	L?	13%	47%	40%	1.733	No Observed Effect Level (NOEL)	Journal	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
115968	Trichlorethyl phosphate	**NL?-L?**	14	50	-3	2.39	NL?	7%	60%	33%	1.733	Reference Dose (RfD)	RAISHE	NCAR	Percentage of Samples (Detects), Surface Water, Ambient	NREC
121142	2,4-Dinitrotoluene	**L?-L**	15	60	+1	3.53	L	38%	54%	8%	2.308	Lifetime Cancer Risk (10^-4)	EPAHA	CAR	Percentage of PWSs (Detects), All Water, Finished	UCMR

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	Set 3 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
121755	Malathion	**NL**	13	77	+3	1.23	NL	31%	54%	15%	2.154	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
122667	1,2-Diphenylhydrazine	**NL-NL?**	12	100	+/-0	1.50	NL?	64%	27%	9%	2.545	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
126987	Methacrylonitrile	**NL**	14	93	+1	1.11	NL	54%	31%	15%	2.385	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
135988	sec-Butylbenzene	**NL?**	15	93	+/-0	2.00	NL?	29%	64%	7%	2.214	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
298044	Disulfoton	**NL**	14	71	+3	1.35	NL	38%	38%	23%	2.154	Reference Dose (RfD)	OPP, 2002	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
309002	Aldrin	**L?**	15	73	+4	3.27	L?	33%	47%	20%	2.133	Lifetime Cancer Risk (10^-4)	EPAHA	CAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
314409	Bromacil	**NL?**	15	73	-4	1.80	NL?	36%	43%	21%	2.143	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
50000	Formaldehyde	**L?-L**	15	67	-3	3.27	L?	13%	47%	40%	1.733	Reference Dose (RfD)	IRIS	NCAR	Release, Number of States	TRI
50997	D-Glucose	**NL?-NL**	14	64	-3	2.14	NL?	8%	8%	85%	1.231	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
75570	Tetramethylammonium chloride	**L?**	14	57	-3	2.77	L?	14%	7%	79%	1.357	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
78002	Tetraethyl lead	**L**	15	73	-2	3.88	L	7%	43%	50%	1.571	Reference Dose (RfD)	IRIS	NCAR	Production Volume	CUS/IUR
78795	Isoprene	**L?-L**	15	47	-7	2.94	L?	7%	21%	71%	1.357	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Production Volume	CUS/IUR
78820	Isobutyronitrile	**L?-L**	15	33	-7	3.00	L?	7%	0%	93%	1.133	Lethal Dose 50 (LD50)	HSDB	NCAR	Production Volume	CUS/IUR
101779	Benzenamine, 4,4'-methylenebis-	**L**	15	67	-5	3.40	L?	13%	47%	40%	1.733	Slope Factor (Oral)	OEHHA	CAR	Release, Number of States	TRI

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	Set 3 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
108930	Cyclohexanol	**L?-L**	14	64	-6	2.83	L?	7%	21%	71%	1.357	Lethal Dose 50 (LD50)	RTECS	NCAR	Release, Number of States	TRI
302012	Hydrazine	**L**	15	87	-1	3.79	L	13%	53%	33%	1.800	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Release, Number of States	TRI
625558	Isopropyl formate	**L**	13	54	-5	3.46	L?	0%	7%	93%	1.071	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
1111780	Ammonium carbamate	**L?**	13	77	-2	2.75	L?	14%	7%	79%	1.357	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
1335326	Lead acetate	**L**	14	50	-6	3.35	L?	8%	17%	75%	1.333	Slope Factor (Oral)	OEHHA	CAR	Production Volume	CUS/IUR
3268493	Methional	**L?**	13	69	-2	2.86	L?	0%	31%	69%	1.308	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
4719044	Hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine	**L**	13	38	-6	3.41	L?	7%	7%	86%	1.214	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
5216251	4-Chlorobenzotrichloride	**L?-L**	14	86	-2	3.21	L?	14%	36%	50%	1.643	NOAEL	OPPT	NCAR	Production Volume	CUS/IUR
6610293	Methylthiosemicarbazide	**L?**	14	71	-2	2.75	L?	0%	15%	85%	1.154	Lethal Dose 50 (LD50)	RTECS	NCAR	Production Volume	CUS/IUR
13463406	Iron pentacarbonyl	**L?-L**	13	62	-6	2.81	L?	0%	31%	69%	1.308	Lethal Dose 50 (LD50)	HSDB	NCAR	Release, Number of States	TRI
23422539	Methanimidamide, N,N-dimethyl-N'-[3-[[(methylamino)carbonyl]oxy]phenyl]-, monohydrochloride	**L?-L**	14	57	-3	3.27	L?	17%	42%	42%	1.750	Reference Dose (RfD)	OPP	NCAR	Release, Number of States	NCFAP
71751412	Avermectin B1	**L?-L**	13	69	-1	3.39	L?	14%	29%	57%	1.571	ADI	JMPR 1997	NCAR	Release, Number of States	NCFAP
91465086	Cyclopropanecarboxylic acid, 3-2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethyl- cyano(3-phenoxyphenyl)methyl ester, 1.alpha.(S*),3.alpha.(Z)-(.+ -.)-	**L?-L**	14	71	-4	3.11	L?	14%	36%	50%	1.643	Reference Dose (RfD)	IRIS	NCAR	Release, Number of States	NCFAP

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	Set 4 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
	Cobalt compounds	**L**	8	75	-2	3.81	L	22%	22%	56%	1.667	Lowest Observed Adverse Effect Level (LOAEL)	Journal	NCAR	Release, Number of States	TRI
51796	Urethane	**L**	8	63	-2	3.79	L	22%	0%	78%	1.444	No Observed Effect Level (NOEL)	Journal	NCAR	Release, Number of States	TRI
55630	Nitroglycerin	**L? - L**	9	78	+/- 0	3.50	L	9%	18%	73%	1.364	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Release, Number of States	TRI
60355	Acetamide	**L**	9	67	-2	3.56	L	20%	20%	60%	1.600	Slope Factor (Oral)	OEHHA	CAR	Release, Number of States	TRI
62533	Aniline	**L? - L**	10	70	+2	3.61	L	20%	30%	50%	1.700	Reference Dose (RfD)	RAISHE	NCAR	Release, Number of States	TRI
67561	Methanol	**L? - L**	10	60	+1	3.45	L?	17%	50%	33%	1.833	Reference Dose (RfD)	IRIS	NCAR	Release, Number of States	TRI
71363	1-Butanol	**L? - L**	11	55	-1	3.33	L?	17%	33%	50%	1.667	Reference Dose (RfD)	IRIS	NCAR	Release, Number of States	TRI
75218	Ethylene oxide	**L**	9	78	-2	3.78	L	36%	18%	45%	1.909	Slope Factor (Oral)	OEHHA	CAR	Release, Number of States	TRI
75569	Propylene oxide	**L**	9	89	-1	3.78	L	36%	18%	45%	1.909	Slope Factor (Oral)	OPP	CAR	Release, Number of States	TRI
76879	Triphenyltin hydroxide	**L**	10	80	-2	3.90	L	22%	44%	33%	1.889	Slope Factor (Oral)	OPP	CAR	Release, Number of States	NCFAP
80159	Cumene hydroperoxide	**L**	10	60	-3	3.61	L	18%	9%	73%	1.455	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Release, Number of States	TRI
106990	1,3-Butadiene	**L**	11	73	-2	3.80	L	27%	9%	64%	1.636	Slope Factor (Oral)	OEHHA	CAR	Release, Number of States	TRI
107211	Ethylene glycol	**L**	10	80	-2	3.70	L	27%	36%	36%	1.909	Reference Dose (RfD)	IRIS	NCAR	Release, Number of States	TRI
109864	2-Methoxyethanol	**L**	9	78	-3	3.65	L	30%	10%	60%	1.700	Reference Dose (RfD)	RAISHE	NCAR	Release, Number of States	TRI
121448	Triethylamine	**L**	7	43	-4	3.36	L?	0%	29%	71%	1.286	Lowest Observed Adverse Effect Level (LOAEL)	RTECS	NCAR	Release, Number of States	TRI

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	Set 4 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
123911	1,4-Dioxane	**L**	9	100	+/-0	4.00	L	30%	30%	40%	1.900	Lifetime Cancer Risk (10^-4)	EPAHA	CAR	Release, Number of States	TRI
133062	Captan	**L**	10	70	-2	3.72	L	33%	22%	44%	1.889	Slope Factor (Oral)	OPP	CAR	Release, Number of States	NCFAP
137304	Ziram	**L**	8	88	-1	3.75	L	13%	25%	63%	1.500	Slope Factor (Oral)	OPP	CAR	Release, Number of States	NCFAP
319846	.alpha.-Hexachlorocyclohexane	**L?**	12	67	+1	3.00	L?	18%	64%	18%	2.000	Lifetime Cancer Risk (10^-4)	IRIS	CAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
330541	Diuron	**NL?**	13	77	+3	2.19	NL?	18%	64%	18%	2.000	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
330552	Linuron	**NL**	12	92	+/-0	1.00	NL	50%	40%	10%	2.400	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
333415	Diazinon	**NL**	11	91	+1	1.09	NL	45%	36%	18%	2.273	Reference Dose (RfD)	OPP	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
541731	m-Dichlorobenzene	**NL?**	13	77	+1	2.00	NL?	45%	45%	9%	2.364	Reference Dose (RfD)	EPAHA	NCAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
542756	Telone	**L?**	13	62	+3	3.23	L?	25%	50%	25%	2.000	Slope Factor (Oral)	OPP	CAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

	Set 4 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
630206	1,1,1,2-Tetrachloroethane	**L?**	13	77	-1	2.88	L?	27%	64%	9%	2.182	Lifetime Cancer Risk (10^-4)	EPAHA	CAR	Percentage of PWSs (Detects), All Water, Finished	NCODR12
759944	S-Ethyl dipropylthiocarbamate	**NL**	12	75	+3	1.38	NL	55%	45%	0%	2.545	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
944229	Fonofos	**NL**	12	83	+/-0	1.00	NL	60%	40%	0%	2.600	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
1313275	Molybdenum oxide (MoO3)	**L**	11	45	-3	3.38	L?	0%	25%	75%	1.250	RfD (UL)	DRI	NCAR	Release, Number of States	TRI
1582098	Trifluralin	**NL - NL?**	11	82	+2	1.59	NL?	56%	44%	0%	2.556	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
1610180	Prometon	**NL**	12	100	+/-0	1.00	NL	40%	40%	20%	2.200	Reference Dose (RfD)	IRIS	NCAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
1634044	Methyl tert-butyl ether	**L?**	12	58	+5	3.42	L?	10%	70%	20%	1.900	Slope Factor (Oral)	OEHHA	CAR	Percentage of PWSs (Detects), All Water, Finished	UCMR
1861321	Chlorthal-dimethyl (Dacthal)	**NL?**	12	67	+4	2.25	NL?	33%	56%	11%	2.222	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA

Appendix F. Chemicals Reviewed by the EPA Evaluation Team: Summary of Results

	Set 4 Summary				Direction - disagree			Overall Confidence				POTENCY Data Element			PREVALENCE Data Element	
CASRN	Common Name	Model Decision	# Evaluators	% agreement	+/- (+ toward L)	Value (L=4; NL=1)	Category	H%	M%	L%	Value H=3; L=1)	Element (L4G)	Source	Type (NCAR / CAR)	Element (L4G)	Source
1897456	Chlorothalonil	**NL?**	12	75	+3	2.17	NL?	20%	60%	20%	2.000	Reference Dose (RfD)	OPP	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
2164172	Fluometuron	**NL**	11	91	+/-0	1.00	NL	20%	70%	10%	2.100	Reference Dose (RfD)	IRIS	NCAR	Percentage of Sites (Detects), All Water, Ambient	NAWQA
26471625	Toluene diisocyanate	**L**	10	80	-1	3.89	L	25%	25%	50%	1.750	Slope Factor (Oral)	OEHHA	CAR	Release, Number of States	TRI

Appendix G. PCCL Contaminants with Incomplete Data for Scoring or that had Parent Compounds Scored

CASRN	Substance Name	Common Name
930552	Pyrrolidine, 1-nitroso-	N-nitrosopyrrolidine (NPYR)
10595956	Ethanamine, N-methyl-N-nitroso-	N-Nitrosomethylethylamine (NMEA)
683181	Stannane, dibutyldichloro-	Dibutyltin dichloride
753731	Stannane, dichlorodimethyl-	Dimethyltin dichloride
818086	Stannane, dibutyloxo-	Dibutyltin oxide
5160021	Benzenesulfonic acid, 5-chloro-2-[(2-hydroxy-1-naphthalenyl)azo]-4-methyl-, barium salt (2:1)	C.I. Pigment Red 53, barium salt (2:1)
7447418	Lithium chloride (LiCl)	Lithium chloride
7782992	Sulfurous acid	Sulfurous acid
7783064	Hydrogen sulfide (H2S)	Hydrogen sulfide
7783188	Thiosulfuric acid (H2S2O3), diammonium salt	Ammonium thiosulfate
12108133	Manganese, tricarbonyl[(1,2,3,4,5-.eta.)-1-methyl-2,4-cyclopentadien-1-yl]-	Methylcyclopentadienyl manganese tricarbonyl
14808607	Quartz (SiO2)	Quartz (SiO2)
75003	Ethane, chloro-	Chloroethane
75025	Ethene, fluoro-	Vinyl fluoride
75887	Ethane, 2-chloro-1,1,1-trifluoro-	HCFC-133a
102716	Ethanol, 2,2',2''-nitrilotris-	Triethanolamine
106876	7-Oxabicyclo[4.1.0]heptane, 3-oxiranyl-	1,2-Epoxy-4-(epoxyethyl)cyclohexane
115117	1-Propene, 2-methyl-	Isobutene
116143	Ethene, tetrafluoro-	Tetrafluoroethene
127060	2-Propanone, oxime	2-Propanone oxime
7440291	Thorium	Thorium-232
10028156	Ozone	Ozone
57018527	2-Propanol, 1-(1,1-dimethylethoxy)-	Propylene glycol mono-t-butyl ether
1007289	1,3,5-Triazine-2,4-diamine, 6-chloro-N-ethyl-	Desisopropylatrazine
1313275	Molybdenum oxide (MoO3)	Molybdenum trioxide
6190654	1,3,5-Triazine-2,4-diamine, 6-chloro-N-(1-methylethyl)-	Desethylatrazine
7681529	Hypochlorous acid, sodium salt	Sodium hypochlorite
79277671	2-Thiophenecarboxylic acid, 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-	Thifensulfuron
76578126	Quizalofop	Quizalofop
56070156	Terbufos-O-analogue sulfone	Terbufos-O-analogue sulfone
	Diazinon oxygen analog	Diazinon oxygen analog
	DCPA mono/di-acid degradate	Dacthal mono/di-acid degradate