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Enhancing the Benefit of the Chemical Mixture Methodology: A Report on Methodology Testing and Potential Approaches for Improving Performance

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January 2012

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Summary

A series of 24 chemical mixtures are used in this study to test the CMM. A dozen chemical mixtures are based on the chemical inventory in a series of laboratories located in at Pacific Northwest National Laboratory (PNNL). These mixtures each contain from seven to 15 chemicals. The other 12 chemical mixtures contain from three to six chemicals that were selected randomly. Three different versions of the CMM are used in testing: 2007 version of the CMM with PAC Revision 21, 2007 version of the CMM with PAC Rev 26, and 2011 version of the CMM with PAC Rev 26.

The first portion of this study focused on how HI values change as a result of enhancements to the PAC data set used in the CMM. For each chemical mixture, the HIs for each individual chemical are added together to produce a cumulative HI for the mixture. Averaging over all 24 test cases, the mean cumulative HI calculated using PAC Rev 21 shows little difference from the mean cumulative HI calculated using PAC Rev 26. However within each individual test case, there was an average of a factor of two difference between in the cumulative HI values computed using the different PAC data sets. This is not surprising given that some PAC Rev 26 values have changed by an order of magnitude or more (sometime upward, sometimes downward) from their PAC Rev 21 values.

The next portion of the study focused on evaluating the benefit of using the Health Code Number (HCN) approach within the CMM. The HCN-based approach is intended to provide a less overly conservative estimate of HIs than the simple summing of the HIs for each chemical in a mixture to generate a cumulate HI value. The "benefit" of using an HCN-based approach for calculating HI values, as opposed to just using the cumulative HI, is determined by taking the difference in the HI values generated using the two approaches and dividing that difference by the cumulative HI value. In the 24 test cases, the 2007 version of the CMM with PAC Rev 21 produced an average benefit of about 11%, with 7 of 24 test cases exhibiting a benefit >10%. The 2007 version of the CMM with PAC Rev 26 produced an average benefit of about 8%, with 3 of 24 test cases producing a benefit >10%. Finally, the 2011 version of the CMM with PAC Rev 26 produced an average benefit of about 4%, with only 2 of 24 test cases having a benefit >10%.

The decrease in the benefit of the HCN-based approach from 2007 to 2011 was initially a concern, but a careful assessment of the data indicated that the current version of the CMM is more accurate than the older version of the CMM. The introduction of new HCN categories and the better characterization of HCNs for all the chemicals in the CMM data set have improved the CMM. In some cases these changes have acted to increase the benefit in from using the HCN-based approach and in other cases these changes have acted to decrease the benefit.

The HCN-based approach is not designed to provide a benefit over the cumulative HI approach for many types of mixtures. No benefit should be seen when there is only one chemical in mixture that is an overwhelming contributor to the cumulative HI value (i.e., accounts for over 95% of the HI) and when there are two or more chemicals in a mixture that are overwhelming contributors to the cumulative HI and they have an overlap in their HCN assignments (i.e., the chemicals have one or more common modes of action or target organ effects). However, the HCN-based approach should provide significant benefits when there are two or more chemicals in a mixture that are significant contributors to the cumulative HI and the chemicals do not have an overlap in their HCN assignments.

In assessing the HCN-based approach, the current method was found to work well in most test cases, but to be overly conservative in a few test cases. This study has identified a number of contributing factors to this tendency towards over-conservatism. The Chemical Mixture working group may wish to consider the lessons learned from this study and use this information to fine-tune the current HCN-based approach. If so, it is recommended that actions be taken to (1) review and enhance the HCN characterization and category structure and (2) review and enhance the method used to calculate the "mode of action" (i.e., "mode of toxicity") and "toxic organ effects " through a more judicious (i.e., weighted) application of HCN-related information.

For the review and enhancement of the HCN characterization and category structure, the following is recommended:

- Continue the ongoing review and reassignment of the generic 3.00 and 4.00 HCNs. Replace these generic values with more specific HCN values when there are sufficient chemical-specific toxicity, health, and safety data to support this action.

- Reassess the mode of action categories to see which categories might be overly specific (e.g., three of the current modes of action categories are related to nervous system impacts) and which might be overly broad (e.g., the *Acute System Effects* and C*hronic System Effects* categories each group-together HCNs from a multitude of weakly-related "body systems", such as the bladder, bones, and nose). A refined set of mode of action categories might reduce over-conservatism while increasing user understanding of how the mode of action categories are linked to human health effects. It would also benefit CMM users if the meaning of the term "mode of action" (which is also called by other names such as: "mode of toxicity", "toxic mode", "endpoint mode", etc.) was more clearly defined and only one name was consistently used for this term in the CMM tools and literature.

- Reassess some of the target organ effect categories to ensure that both toxin and irritant effects are considered when estimating health effects to specific target organs. Currently, for some organ systems (e.g., the respiratory system), irritation and toxins are considered together when computing the target organ effect. For other organ systems (e.g., eyes, skin), irritation is ignored and only the impact of toxins are considered when computing the target organ effect.

The reassessment of the HCN category structure can be addressed by holding one or more technical teleconferences/web conferences for the key technical representatives on the Chemical Mixtures working group. Changes made to these category assignments can be easily implemented in the CMM workbook. The goal of these changes would be to improve the accuracy, understandability, and consistency of the CMM's HCN-based approach.

For the review and enhancement of the method used to calculate of mode of action and toxic organ effects, the goal should be to reduce over-conservatism. This can be accomplished by applying *weighting factors* to HCNs based on their relative contributions to the mode of action and target organ effects. The introduction of these weighting factors would allow us to depart from the overly conservative assumption that *all the HCNs identified for a chemical produce their health effect at the chemical's concentration limit.* In reality, only a small subset of the HCNs identified for a chemical might cause detectable health effects at the concentration limit. Health effects associated with many of the HCNs assigned to a chemical will only be observed at much higher chemical concentrations. The challenge in reducing this over-conservatism is to identify, for each chemical, those HCNs that deserve

full weighting at the concentration limit and those HCNs that should be given a lower weighting at this limit.

Several easy-to-implement candidate approaches involving the use of weighting factors have been developed and tested using 12 sets of chemical mixtures. These approaches involve different methods of prioritizing and weighting the HCNs assigned to each chemical. One thing the new, easy-to-implement, candidate approaches have in common is they assign higher weighting factors to acute effects and lower weighting factors to chronic effects. Although chronic effects are less important than acute effects for emergency management applications, chronic effects cannot be totally discounted because some concentration limits, like PAC-2, consider both the impairment of an individual's short-term ability to take protective actions and "irreversible or other serious, long-lasting, adverse health effects".

All of the tested, easy-to-implement approaches provided an average increase in benefit over the current version of the CMM. However, "Approach 1" appears to provide more benefit than warranted by the properties of the chemicals in the mixtures. "Approach 2-Alpha" and "Approach 2-Beta" appear more conservative, with Approach 2-Beta providing the more appropriate level of conservatism. The downside to these new approaches is that without detailed information on which HCNs produce health effects at the chemical's concentration limit, these new approaches may, for some chemicals, apply too low a weighting factor to one or more of the applicable HCNs. On the plus side, Approach 1, 2-Alpha, and 2-Beta would all be easy to implement because they require no changes to the CMM data set, only the introduction of a simple macro in the CMM workbook to set the priority order for the HCNs and minor modifications to the macros used to calculate the HIs for a mixture's mode of action and target organ effects.

In addition to the easy-to-implement approaches, two more-advanced candidate approaches have been identified. These are the "Exposure Route Approach" and the "Primary/Secondary/Tertiary (PST) Approach". Neither of these approaches has yet been fully tested. The Exposure Route Approach bases its weighting factors on the chemical exposure routes (e.g., inhalation, oral) in the studies used to derive the chemical's concentration limits. It also applies a second weighting factor to each chemical's HCNs, following a rank ordering as used in Approach 2. The PST Approach is the most sophisticated; it prioritizes and weights the HCNs based on their likely contribution to the health effects observed in the studies used to derive each chemical's concentration limits.

It would involve only a cursory review of existing HCN-derivation literature by our research interns to acquire the information needed to implement the Exposure Route Approach. The PST Approach would require the most work to implement because it would involve having the research interns review existing HCN-derivation and related PAC literature. On the plus side, the PST approach would maintain an appropriate level of conservatism and provide the highest level of technical defensiveness of any of the potential HCN-based approaches.

To implement the review and enhancement of the method used to calculate of mode of action and toxic organ effects, the following recommendations are proposed:

- Additional testing should be conducted on easy-to-implement enhancements to the CMM's HCN-based approach. The objective would be to identify and thoroughly assess a method for implementing HCN weighting factors that could serve as a near-term option for enhancing the performance of the CMM's HCN-based approach.

- Initial testing should be conducted by the CMM program's research interns on the proposed Exposure Route and PST approaches. The goal would be to gauge the benefit of these approaches and clearly ascertain the level of effort that would be required to gather the information needed to fully implement one of these two long-term approaches.

- NA-41 and the Chemical Mixtures working group should discuss the results of the next phase of testing and, if warranted, develop a plan and schedule for implementing cost-effective enhancements to the CMM's HCN-based approach. Through the use of national laboratory research interns, many enhancements to the current approach should be implementable at a minimal cost to the CMM program.

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The authors are indebted to the DOE Office of Emergency Management and Policy's (NA-41) Jim Fairobent and Dave Freshwater for the support, encouragement, and sponsorship of the CMM.

Finally, the senior members of the research team acknowledge the hard work, dedication, and creativity invested in this project by our research interns. The tireless efforts of Juan Yao, Hua He, Alex Booth, Phil Bouslaugh, and Donna Trott have been invaluable in advancing and updating the CMM. We acknowledge the contributions made by a variety of US Department of Energy and Pacific Northwest National Laboratory science education programs in sponsoring the work by our interns.

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1.0 Introduction

In the spring of 2011, members of the Chemical Mixture Methodology (CMM) development team at Pacific Northwest National Laboratory (PNNL) began conducting in-depth testing to quantify the benefit of using the CMM's Health Code Number (HCN) approach. As part of this effort, several candidate enhancements to the HCN-based approach were proposed and tested. This report presents the findings of this research effort.

This report is intended for use by the Department of Energy (DOE) Office of Emergency Management and Policy (NA-41) and members of the DOE Subcommittee on Consequence Assessment and Protective Actions (SCAPA) Chemical Exposure and Chemical Mixtures Working Group. The goal of this study is to better understand the performance of the current CMM's HCN-based approach and begin the process of exploring potential enhancements to the CMM that will improve its usefulness while maintaining an appropriate level of conservatism for emergency management applications. With NA-41 spearheading efforts to implement a major revision in the process used to derive the Temporary Emergency Exposure Levels (TEELs), this seems like an opportune time to assess the performance of the CMM.

This report presents:

- Background information on the CMM, its HCN-based approach, and a method to evaluate the benefit derived from using the HCN-based approach.

- The results of CMM testing using twenty-four chemical mixtures. The CMM testing involves using two different "flavors" of the 2007 version of the CMM and the 2011 version of the CMM.

- The description and testing of two new, easy-to-implement approaches for enhancing the 2011 version of the CMM. These new approaches were proposed for testing by members of SCAPA's Chemical Mixtures Working Group.

- The description of a couple of more-sophisticated approaches for enhancing the CMM. These approaches are intended to increase the benefit of the HCN-based approach while still ensuring an appropriate level of conservatism is maintained.

- Recommendations are proposed, which are intended to serve as conversation starters for discussions involving NA-41 and by the Chemical Mixtures Working Group about the next steps for considering potential future enhancements to the CMM.

Most of the technical work presented in this report was conducted by two PNNL masters-level interns, Hua He and Juan Yao. Xiao-Ying Yu and Cliff Glantz provided mentorship, technical guidance, and writing support to the interns. Alex Booth (another PNNL research intern) also provided technical analyses for this effort.

2.0 Testing Strategy

Emergency preparedness personnel at DOE facilities use the CMM to estimate the potential health impacts to workers and the public from the airborne release of chemical mixtures. Developed and maintained under the sponsorship of the DOE's NA-41, the CMM is recommended for use in emergency preparedness and response and safety analysis decision making in the DOE complex in accordance with DOE Order 151.1C (DOE, 2005).

The CMM assesses mixtures of potentially hazardous chemicals that are separable into their component elements or compounds by pure physical processes. The individual chemicals may have been stored as a mixture prior to the event that initiated their atmospheric release, or they may have been stored separately and only mixed after their release to the atmosphere. The CMM does not account for any chemical reactions that may occur in the atmosphere as the mixture is transported away from its source. One of the assumptions of the CMM is that the health impacts from exposure to each chemical in mixture are additive – potential synergistic and antagonistic effects are not considered (Craig *et al.,* 1999).

There are several recent documents that describe how the CMM works (e.g., Craig et al., 2011 and Yu et al., 2010). The first step performed by the CMM is to calculate the **hazard index (HI)** for each chemical species (i) at a receptor location, as shown in eqn. 1:

$$HI_i = C_i / L_i \qquad \text{eqn. 1}$$

where C_i is the concentration of chemical "i" at the receptor and L_i is the selected concentration limit.

The DOE recommends using **Protective Action Criteria (PAC) values**[a] as concentration limits, either PAC-1, -2, or -3 for chemical "i" (i.e., $L_i = PAC_i$). The PAC-1 limit is the lowest concentration associated with mild, transient health effects. The PAC-2 limit is the lowest concentration associated with irreversible or other serious health effects that could impair the ability to take protective action. The PAC-3 limit is the lowest concentration associated with life-threatening health effects.

If $HI_i < 1.0$, the concentration of the chemical "i" does not exceed its concentration limit. If PAC-2 is being used as the concentration limit, exposed individuals should not experience any health effect that would impair their ability to take effective protective actions. However, if $HI_i \geq 1.0$, the chemical concentration would equal or exceed the PAC-2 limit, and the exposed individual may experience health effects that could impair their ability to take effective protective actions.

In a chemical mixture, the HI_i for each chemical at a receptor point of interest can be summed, as in eqn 2.

$$\sum_{i=1}^{n} HI_i = HI_1 + HI_2 + \cdots + HI_n \qquad \text{eqn. 2}$$

[a] The PAC data set, PAC searchable database, and technical information on the PAC are available at http://www.atlintl.com/DOE/teels/teel.html.

This cumulative HI, $\sum_{i=1}^{n} HI_i$, provides a simple but often overly conservative estimate of health effects when the chemicals in the mixture impact different body systems.

Another simple approach for estimating the health effects from exposure to chemical mixtures is to treat each chemical in the mixture as if there are no additive health effects from the exposure to each chemical in the mixture. In this approach, only the maximum health effect from any single chemical in the mixture is assumed to represent the health effect from exposure to the mixture (i.e., the health effects from exposure to the other chemicals in a mixture is discounted). This approach is non-conservative and can substantially underestimate human health impacts.

An alternative to these two approaches is the HCN-based approach that is incorporated into the CMM. This approach involves using HCNs to combine identical or similar health effects from all the chemicals in the mixture, while not combining unrelated health effects. HCNs are similar to medical diagnostic codes in that they are code numbers that identify specific acute or chronic toxic effects involving individual **modes of action** in the body (also called **modes of toxicity**) and **target organ effects**. These terms refer to the combined toxic effect on a specific organ or tissue (e.g., "acute kidney toxin", "acute bone marrow toxin) or their combined effect in producing a particular mode of action that may involve multiple organs or tissues (e.g., "acute systemic toxins", "acute nervous system effects").

Currently, 60 different HCNs are available for characterizing the potential modes of action and target organ effects associated with exposure to a chemical. This includes the addition of 16 new HCNs since the 2007 version of the CMM was issued; including 13 new "acute HCNs" that were added to mirror the chronic target organ HCNs used in earlier versions of the CMM. Before the new acute HCNs were added, the CMM used chronic HCNs as "surrogates" to represent potential acute effects. The addition of the new acute HCNs allows a more representative and explicit characterization of potential acute effects from an unplanned release.

HCNs are assigned to each chemical in the CMM data set. The HCN-based approach in the CMM assumes that the HIs from different chemicals are additive only if the chemicals have HCNs that impact the same modes of action or target organ effect categories (see eqn. 3). Further, acute and chronic health effects to the same target organ set are not considered additive because these impacts occur over different time scales.

$$\sum_{i=1}^{n} HI_{i(p)} = HI_{1(p)} + HI_{2(p)} + \cdots + HI_{n(p)} \qquad \text{eqn. 3}$$

Note: "p" represents a specific target organ or mode of action.

Because the HCN-based approach focuses on health effects involving common modes of action and target organ effects, it may produce HI values that are less than the cumulative HI value. This should in some cases produce conservative, but less overly conservative, estimates.

In this paper, we have used the term "*benefit*" to describe the reduction in HIs that are achieved by applying the CMM using the HCN-based approach rather than simply using cumulative HIs. Equation 4 indicates how this benefit is calculated for a given mode of action or target organ effect.

$$Benefit(p) = \frac{\sum_{i=1}^{n} HI_i - \sum_{i=1}^{n} HI_{i(p)}}{\sum_{i=1}^{n} HI_i} * 100\% \quad \text{eqn. 4}$$

The overall benefit of the HCN-based approach is determined by taking the smallest benefit[a] found in any of the mode of action or target organ effect categories.

A Simple Illustration of the Benefit in Using the HCN-based Approach

Consider the following two chemical mixture scenarios:

Scenario 1. Two chemicals are released to the atmosphere and each chemical is an acute nervous system toxin (HCN=7.00). An HI of 0.6 is computed for each chemical at the receptor location.

Scenario 2. Two chemicals are released to the atmosphere and one chemical is an acute nervous system toxin (HCN=7.00) and the other is an acute bladder toxin (HCN=4.03). They have no overlap in any HCN category. An HI of 0.6 is computed for each chemical at the receptor location.

Under Scenario 1, the cumulative HI is 1.2. The sum of the HIs for acute nervous system effects is also 1.2. The benefit from using the HCN-based approach in Scenario 1 is 0%.

Under Scenario 2, the cumulative HI is 1.2. With the two chemicals having different modes of action (and impacting different target organ systems), the largest HI for any mode of action or target organ is 0.6. The benefit from using the HCN-based approach in Scenario 2 is 50%.

Although screening using the cumulative HI indicates that both scenarios may be of concern, the HCN-based approach clarifies that from an emergency management perspective, Scenario 1 is a concern while Scenario 2 is not.

In applying the CMM to a chemical mixture, the following information is required:

1. Name and CASRN number of each chemical in the mixture (this information can be obtained from the CMM's PAC data set)

2. The estimated concentration of each chemical in the mixture at a user-specified receptor location (as typically determined through the use of an atmospheric dispersion model). This information is input by the user.

3. A health-based concentration limit for the exposure to each chemical. The same type of concentration limit must be used for each chemical in the mixture, though the actual value of that limit

[a] The smallest benefit is associated with the largest $\sum_{i=1}^{n} HI_{i(p)}$ value in eqn. 4.

will vary from chemical to chemical. The default CMM uses either PAC-1, -2, or -3 values to provide the concentration limit for each chemical. PAC-1, -2, and -3 values are defined for each of the chemicals listed in the CMM workbook's data set. PAC-2 is most often used in CMM analyses because it represents a chemical exposure level that could impair an individual's ability to take protective actions (DOE, 2005; Appendix F of DOE, 2007). The CMM can be modified to use different concentration limit values in place of PACs.

4. The HCNs assigned to each chemical indicate which target organ groups are impacted by exposure to that chemical. HCNs offer a convenient way of categorizing identical or similar target organ effects. Like PAC values, HCN values are provided for each chemical in the CMM data set. Up to 10 HCNs are listed to each chemical in the current CMM workbook, with these HCNs evaluated from literature reviews according to the HCN development procedure and selected based on the generic priority order of their health effects. The ranking of health effects was developed in part by using national vital statistics data for the year 2000 for death from various causes published by the National Center for Health Statistics (Minino and Smith, 2001). HCN health effects were initially ranked in the order of their seriousness, from serious bodily injury or death in a fraction of a second to generally low-risk health effects. The rankings were then adjusted to incorporate the impact of the health effect on a person's ability to take protective action in an emergency situation. As a result, some health effects (e.g., a moderate skin irritation) that have negligible long-term consequences but may hinder protective actions can have a higher ranking than those HCNs that involve more significant long-term consequences (e.g., chronic liver effects) but may not immediately hinder an individual's capability to evacuate or take other protective actions.

All of the above, except the HCN assignments, are used to compute the cumulative HI for each chemical at the designated receptor location. The cumulative HI can be considered a **CMM screening approach** for estimating health effects. If the cumulative HI < 1.0, no further assessment is typically needed because this overly conservative method is indicating that cumulative HI would not be at a level of immediate concern (e.g., impaired ability to take protective actions, mild or transient health effects). If the cumulative HI ≥ 1.0, the HCN-based approach can be applied to determine if the HI is less than 1.0 for the most effected mode of action or target organ.

All chemicals in the CMM database have been reviewed over the past few years and the new HCN categories and priority ranking have been applied. In most cases, this review has resulted in an increase in the number of HCNs assigned to each chemical. Also, more specificity has applied to the HCN data, so that while there may be more HCNs assigned to a given chemical, there is a reduced usage of broad, non-specific HCN catch-all categories. To illustrate, in the 2007 version of the CMM, the broad HCN of 4.00 (acute systemic toxin) was assigned to over 1,000 chemicals in the data set (about a third of all the chemicals in the data set). In the 2011 version of CMM, less than 400 chemicals still were assigned an HCN or 4.00. A chemical assigned an HCN of 4.00 in the past, might now be assigned more specific HCNs such as 4.04, 4.06, and 4.08 (acute bone marrow, hematological, and cardiovascular system effects, respectively).

3.0 CMM Testing and Benefit Analysis

This section reports on testing of the CMM. The test cases are described and results are presented for the cumulative HI and the HCN-based approach. The benefit of using the HCN-based approach is analyzed and key observations are presented.

3.1 CMM Test Cases

A series of 24 chemical mixtures are used to test the CMM. The first 12 of these chemical mixtures are based on the reported chemical inventory in a series of laboratories located in PNNL's Sigma V Building. Each of these test cases features from seven to 15 chemicals in the studied mixture.

Tables 1a and **1b** present the test case number and name, the cumulative HIs computed by the CMM using PAC Revision (Rev) 21 and 26, and the name of each chemical in the mixture. The total inventory of each chemical is assumed to be released to the atmosphere. This overly conservative assumption is made to bring the cumulative HI for most of the mixtures into the range between 0.1 and 10. The concentration of each chemical at the designated receptor is determined through atmospheric dispersion modeling (e.g., using EPICode, a model approved by DOE for safety assessments).

The second set of 12 chemical mixtures is obtained through the random selection of chemicals from the PAC Rev 26 data set. Each of these 12 test cases involves six related pairs of chemical mixtures. The first mixture in each test case pairing is made up of three randomly selected chemicals. The second mixture in each pair adds up to three additional randomly-selected chemicals to the three chemicals that make the first mixture in the pairing.

The random selection of chemicals is accomplished using a random number generator. In the event a randomly selected chemical is in PAC Rev 26 but not in PAC Rev 21, that chemical is rejected. For each test case, two replacement chemicals (these are also randomly selected) are available to stand in for any rejected chemical. Although a total of six chemicals are preferred for the second mixture in each pairing, five chemicals are used when the number of rejected chemicals exceeds the number of available replacement chemicals.

Tables 2a and **2b** present basic information for this second group of 12 chemical mixtures. An identical amount of each chemical is assumed to be released to the atmosphere in this round of 12 test cases. A concentration of 3.5 mg/m^3 was assumed at the designated receptor for each chemical in the mixtures.

3.2 CMM Testing Results: Cumulative HI Values

Table 3 presents the results of the CMM analysis for the first 12 test cases and **Table 4** presents results for the second set of 12 test cases. These tables present and contrast CMM analyses using the:

- 2007 Version of the CMM using PAC Rev 21
- 2007 Version of the CMM using PAC Rev 26
- 2011 Version of the CMM using PAC Rev 26.

Table 1a. Chemicals that Form the Mixtures in the First Six Test Cases.

1. Room 1411		2. Rm. 1415: Case 1		3. Rm. 1415: Case 2		4. Room 1419		5. Room 1423		6. Room 1514	
∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26
7.0	2.8	2.1	1.7	41	23	4.3	4.2	1.8	2.1	6.5	6.0
Sodium glycolate; (Sodium hydroxyacetate)		Calcium chloride dihydrate		Silica, crystalline-quartz; (Silicon dioxide)		Cyclopropane		Trichloroacetic acid		Tributyl phosphate	
Potassium cyanide		Carbon; (Graphite, synthetic)		Lithium bromide		Iron(II) chloride tetrahydrate		Citric acid		Phthalic acid	
Dichloroethylene, cis-and trans-1,2-		Sodium oxalate		Sodium chloride		Ethylene oxide; (Oxirane)		Agar		Potassium phosphate, monobasic	
Ethylene glycol		Sodium metabisulfite		Sodium phosphate, tribasic		Acrylic acid polymers; (Acrylic polymer or resin)		Boric acid		Nickel sulfate hexahydrate	
Propionic acid		Sodium bromide		Sulfuric acid		Iron		Magnesium chloride		Ammonium acetate	
Phenanthrene		Magnesium carbonate; (Magnesite)		Hydrogen chloride; (Hydrochloric acid)		Potassium chloride		Potassium chloride		Ethylenediaminetetraacetic acid, disodium salt	
Lactic acid		Zinc acetate		Phosphoric acid		Sodium perrhenate; (Rhenium(VII) sodium oxide)		Sodium carbonate		Cupferron; (Ammonium-n-nitrosophenylhydroxylamine)	
Oxalic acid, dehydrate		Ammonium thiocyanate		Hexane		Palladium		Sodium phosphate, tribasic		Sodium gluconate	
Potassium phosphate, dibasic		Sodium phosphate, tribasic		Phthalic acid				Sodium hydroxide		Ammonium formate	
Magnesium chloride		Sulfur		Mercury vapor				Sodium bicarbonate		Adipic acid	
Chromic oxide (Chromium(III) oxide)				Iron				Lithium hydroxide			
Potassium phosphate, monobasic				Sodium sulfite				Potassium ferricyanide			
Lead chromate				Methylene chloride				Manganese(II) chloride (1:2); (Manganous chloride)			
Sodium carbonate				Sodium bromide				Molybdenum trioxide			
Sodium sulfate				Hydroxylamine chloride; (Hydroxylamine hydrochloride)							

Table 1b. Chemicals that Form the Mixtures in the Test Cases 7-12.

7. Room 1518		8. Rm. 1519: Case 1		9. Rm 1519: Case 2		10. Rm. 1519: Case 3		11. Room 1522		12. Outside the Rms.	
∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26
7.5	48.6	1.8	1.7	2.0	1.4	1.9	4.1	2.6	2.8	6.4	6.3
Barium hydroxide		Silica, crystalline-quartz; (Silicon dioxide)		Strontium nitrate		Dimethylacetamide, n,n-		Sodium phosphate, tribasic; (Sodium hexametaphosphate)		Ethyl hexanoic acid, 2-; (Butyl ethyl acetic acid)	
Zinc chloride		Ascorbic acid		Cesium chloride		Pentane, n-		Sodium chloride		Calcium carbide	
Silica amorphous hydrated		Perchloroethylene; (Tetra chloroethylene)		Ferric ammonium sulfate; Sulfuric acid, ammonium iron(3e+) salt(2:1:1)		Methyl alcohol; (Methanol)		Sodium nitrite		Chlorodifluoromethane; (Freon 22; CFC 22)	
Sodium hydride		Tris-hydroxymethylamino methane; (THAM)		Ferric chloride		Copper(II) sulfate pentahydrate		Potassium bromide		Hexane	
Sulfur dioxide		Calcium(II) nitrate tetrahy drate (1:2:4)		Sodium bicarbonate		Toluene		Sodium nitrate		Methyl alcohol; (Methanol)	
Sodium hydroxide		Sodium sulfate, anhydrous		Gallium		Dimethyl sulfoxide; (DMSO)		Calcium chloride dihydrate		Acetonitrile	
Hydrazine hydrate; (Hydrazine monohydrate)		Sodium carbonate		Silver nitrate		Isopropyl alcohol		Potassium nitrate		Isopropyl alcohol	
		Sodium chloride		Sodium chloride		Acetonitrile		Tetrasodium pyrophosphate		Ethylene glycol	
		Potassium chloride		Potassium carbonate		Methylene chloride				Acetone	
		Sodium hydroxide		Sulfur		Chloroform				Xylenes	
		Potassium permanganate		Diphenyl; (Biphenyl)		Tetrahydrofuran				Ethyl acetate	
		Potassium hydroxide		Sodium acetate		Pyridine					
		Ascorbic acid		Tris-hydroxymethylaminometh ane; (THAM)		Ethyl ether					
		Magnesium chloride		Ammonium, hexadecyltrimethyl-, bromide		Dimethylformamide, N,N-					
		Manganese(II) chloride (1:2); (Manganous chloride)		Aluminum oxide; (Alumina)		Cyclohexane					

Table 2a. Chemicals that Form the Mixtures in Test Sets 13-18

13. Set 1a		14. Set 1b		15. Set 2a		16. Set 2b		17. Set 3a		18. Set 3b	
∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26
30.2	30.2	31.5	32.8	1.0	1.0	4.5	1.1	1.6	3.2	1.6	3.2
Trichloroacetic acid		Trichloroacetic acid		Butanenitrile; (Butyronitrile)		Butanenitrile; (Butyronitrile)		Bromochlorobenzene, p-		Bromochlorobenzene, p-	
Methylphenol, 4-; (p-Cresol)		Methylphenol, 4-; (p-Cresol)		Phenylene diisocyanate, 1,4-		Phenylene diisocyanate, 1,4-		Ceric ammonium nitrate		Ceric ammonium nitrate	
Mercury hydroxide		Mercury hydroxide		Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)		Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)		Sodium nickel oxide (Liquid)		Sodium nickel oxide (Liquid)	
		Sodium nickelate (Liquids)				Dichlorobenzene, p-				Thorium oxide; (Thorium dioxide)	
		Glyceryl monostearate; (Octadecanoic acid, monoester with 1,2,3-propanetriol)				Polychlorinated biphenyl (Aroclor 1016); (Chlorodiphenyl (41% Cl))				Diethylene glycol diacetate; (2,2'-oxybisethanol diacetate)	
		Methyl thiocyanate								Barium sulfate	

Table 2b. Chemicals that form the Mixtures in Test Sets 19-24

19. Set 4a		20. Set 4b		21. Set 5a		22. Set 5b		23. Set 6a		24. Set 6b	
∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26	∑HI Rev21	∑HI Rev26
0.1	0.9	0.9	1.7	0.3	0.4	1.3	1.1	0.6	1.0	0.9	1.2
Pentachloroethane		Pentachloroethane		Oxalic acid, anhydrous; (Ethanedioic acid)		Oxalic acid, anhydrous; (Ethanedioic acid)		Ferric nitrate		Ferric nitrate	
Sodium cacodylate; (Sodium dimethylarsinate)		Sodium cacodylate; (Sodium dimethylarsinate)		Trimethylpyridine, 2,4,6-		Trimethylpyridine, 2,4,6-		Bismuth		Bismuth	
Tris-hydroxymethylaminomethane; (THAM)		Tris-hydroxymethylamino-methane; (THAM)		Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)		Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)		Trimethoxysilane		Trimethoxysilane	
		Hexanol, n-; (n-Hexyl alcohol)				Chlorthiophos				Zirconium silane	
		Trimethyloctane, 2,4,6-				Potassium chromate(VI)				Silicon(II) oxide; (Silicon oxide)	
		Strychnine sulfate (2:1)									

Table 3. CMM Analysis for Test Cases 1 -12. HI data are presented using the 2007 Version of the CMM with PAC Rev 21, 2007 Version of the CMM with PAC Rev 26, and the 2011 Version of the CMM with PAC Rev 26. In the columns presenting "Percentage Benefit" data, values ≥ 10% are presented in blue font and values ≥ 20% are presented in red font.

												Percentage Benefit			Percentage Benefit		
		A			B			C				100% * (A-B)/A			100% * (A-C)/A		
		Cumulative HI		$A_{Rev\ 26}$ /	Max HI Value			Max HI Value				Max HI Value			Max HI Value		
				$A_{Rev\ 21}$	Mode of Toxcity			Target Organ				Mode of Toxcity			Target Organ		
	CMM Version:	2007	2007 or 2011		2007	2007	2011	2007	2007	2011		2007	2007	2011	2007	2007	2011
	PAC Rev:	21	26		21	26	26	21	26	26		21	26	26	21	26	26
#	Test Cases																
1	Rm 1411	7.0	2.8	0.4	6.1	1.9	2.4	6.1	1.9	2.4		13%	32%	12%	13%	30%	12%
2	Rm 1415-1	2.1	1.7	0.8	2.0	1.6	1.7	2.0	1.6	1.6		8%	3%	0%	8%	3%	4%
3	Rm 1415-2	40.9	22.9	0.6	33.8	15.8	22.9	37.4	19.4	20.9		17%	31%	0%	9%	15%	9%
4	Rm 1419	4.3	4.2	1.0	4.1	4.0	4.1	4.3	4.2	4.0		5%	5%	0%	0%	0%	5%
5	Rm 1423	1.8	2.1	1.2	1.8	2.1	2.1	1.8	2.1	2.1		2%	2%	0%	1%	0%	0%
6	Rm 1514	6.5	6.0	0.9	4.3	3.8	5.1	6.3	5.8	5.1		34%	36%	15%	3%	3%	15%
7	Rm 1518	7.5	48.6	6.5	7.3	48.4	48.6	7.5	48.6	48.1		2%	0%	0%	0%	0%	1%
8	Rm 1519	1.8	1.7	1.0	1.6	1.6	1.7	1.8	1.7	1.7		9%	9%	0%	0%	0%	1%
9	Rm 1519-2	2.0	1.4	0.7	1.8	1.3	1.4	1.8	1.3	1.3		12%	8%	0%	12%	8%	1%
10	Rm 1519-3	1.9	4.1	2.2	1.5	3.8	4.1	1.7	3.9	4.1		19%	7%	0%	11%	5%	0%
11	Rm 1522	2.6	2.8	1.1	2.6	2.7	2.8	2.6	2.7	2.7		2%	2%	0%	2%	2%	2%
12	Outside	6.4	6.3	1.0	5.7	5.6	6.3	5.4	5.4	6.3		11%	11%	0%	16%	15%	0%
	Average:	7.1	8.7	1.4				Average Benefit (%):				11%	12%	2%	6%	7%	4%

Table 4. CMM Analysis for Test Cases 13-24. HI data are presented using the 2007 Version of the CMM with PAC Rev 21, 2007 Version of the CMM with PAC Rev 26, and the 2011 Version of the CMM with PAC Rev 26. In the columns presenting "Percentage Benefit" data, values ≥ 10% are presented in blue font and values ≥ 20% are presented in red font.

		A			B			C			Percentage Benefit 100% * (A-B)/A			Percentage Benefit 100% * (A-C)/A		
		Cumulative HI		$A_{Rev\ 26}$ / $A_{Rev\ 21}$	Max HI Value Mode of Toxcity			Max HI Value Target Organ			Max HI Value Mode of Toxcity			Max HI Value Target Organ		
	CMM Version:	2007	2007 or 2011		2007	2007	2011	2007	2007	2011	2007	2007	2011	2007	2007	2011
	PAC Rev:	21	26		21	26	26	21	26	26	21	26	26	21	26	26
#	Test Cases															
13	Rnd. Set 1A	30.2	30.2	1.0	30.2	30.2	30.2	30.2	30.2	30.2	0%	0%	0%	0%	0%	0%
14	Rnd. Set 1B	31.5	32.8	1.0	31.2	32.3	32.8	30.3	32.8	32.8	1%	1%	0%	4%	0%	0%
15	Rnd. Set 2A	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	3%	3%	0%	0%	0%	0%
16	Rnd. Set 2B	4.5	1.1	0.2	4.4	1.0	1.1	4.5	1.1	1.1	3%	9%	0%	0%	1%	0%
17	Rnd. Set 3A	1.6	3.2	2.0	1.6	3.2	3.2	1.6	3.2	3.2	0%	0%	0%	0%	0%	0%
18	Rnd. Set 3B	1.6	3.2	2.0	1.6	3.2	3.2	1.6	3.2	3.2	1%	2%	2%	1%	2%	0%
19	Rnd. Set 4A	0.1	0.9	8.9	0.1	0.9	0.9	0.1	0.9	0.9	10%	1%	0%	10%	1%	1%
20	Rnd. Set 4B	0.9	1.7	1.9	0.9	1.6	1.7	0.9	1.6	1.6	1%	1%	0%	1%	1%	1%
21	Rnd. Set 5A	0.3	0.4	1.3	0.3	0.4	0.4	0.3	0.4	0.3	6%	5%	0%	0%	0%	28%
22	Rnd. Set 5B	1.3	1.1	0.8	1.3	1.1	1.1	1.3	1.1	0.8	1%	2%	0%	0%	0%	25%
23	Rnd. Set 6A	0.6	1.0	1.6	0.4	0.8	0.9	0.4	0.9	0.9	42%	12%	9%	27%	2%	9%
24	Rnd. Set 6B	0.9	1.2	1.4	0.6	1.1	1.1	0.7	1.2	1.1	37%	14%	7%	26%	7%	7%
	Average:	6.2	6.5	1.9				Average Benefit (%):			9%	4%	2%	6%	1%	6%

The use of these three versions of the CMM allows us to examine both the impact of changes in the PAC data set and changes in the HCN categories and their chemical-specific assignments on CMM results.

In **Tables 3** and **4**, the first set of data columns ("A") provides the cumulative HI values using the different CMM data sets. Cumulative HI values obtain using PAC Rev 26 data are the same regardless of whether the 2007 or 2011 version of the CMM is used. This is because the cumulative HIs are only a function of chemical concentration and the PAC limit, and are not based on the HCN assignments that vary between the 2007 and 2011 versions of the CMM. For each test case, Appendix A provides the HCN assignments, PAC-2 value, and HI value for each chemical in the mixture. Information is provided for both the 2007 and 2011 versions of the CMM.

Over all the test cases, the average cumulative HI is slightly higher when using PAC Rev 26, but not significantly (i.e., only 13% higher). Looking at each test case separately, the average change in the cumulative HI between using the PAC Rev 21 data set and the PAC Rev 26 data set was a factor of two. This is a fairly large change from an emergency planning perspective. In 19 of the 24 test cases the cumulative HI values using PAC Rev 26 are at, or within a factor of two of those obtained using PAC Rev 21. In three test cases (7.00, 10.00, and 19.00), the cumulative HIs using PAC Rev 26 are more than a factor of two greater than their corresponding PAC Rev 21 values (i.e., factors of 6.5, 2.2, and 8.9, respectively). In two test cases (1 and 16), the cumulative HI values using PAC Rev 26 are less than half their corresponding PAC Rev 21 values (i.e., factors of 0.4 and 0.1, respectively). All the test cases that showed significant changes in cumulative HI values are associated with large changes (i.e., one to two orders of magnitude) from Rev 21 to Rev 26 in the PAC value for at least one of the chemicals in the mixture.

Examples of How Significant Changes in PAC Values Impact HI Values

Consider Test Case 7. As shown in Figure A.7, The PAC-2 value for hydrazine hydrate decreased from 0.063 mg/m^3 (in PAC Rev 21) to 0.0075 mg/m^3 in (PAC Rev 26). This order of magnitude decrease in the PAC increased the HI value for hydrazine hydrate from 5.6 (in PAC Rev 21) to 46.7 (in PAC Rev 26).

Consider Test Case 16. As shown in Figure A.16, the PAC-2 value for lead chromate increased from 1.0 mg/m^3 (in PAC Rev 21) to 93.2 mg/m^3 (in PAC Rev 26). This two orders of magnitude increase in the PAC lowered the HI value for lead chromate from 3.5 (in PAC Rev 21) to 0.04 (in PAC Rev 27)

3.3 CMM Testing Results: Benefits Using the HCN-Based Approach

The CMM's HCN-based approach is designed to provide a less overly conservative estimate of the HI for certain types of chemical mixtures. **Tables 3** and **4** present information on the benefit obtained from using the HCN-based approach, rather than simply using cumulative HI values, in each of the 24 test

cases. If a significant benefit is achieved using the HCN-based approach, this could have an impact on emergency management decisions. For example, the storage of additional quantities of chemicals could be permitted in a given facility. Alternatively, the potential location of a facility fence line could be moved closer in reducing construction and operation costs while still maintaining an appropriate safety margin.

An assessment of HCN-based HI values for test cases 1-12, show that the use of 2007 version of the CMM with PAC Rev 21 produces an average benefit of 11% and 6% for the mode of action and target organ effects, respectively (as presented in columns "B" and "C" columns in **Tables 3** and **4**). Taking the smaller of the mode of action and target-organ effects[a] benefits, four of the 12 test cases produce a benefit of more than 10%. Using the 2007 version of the CMM with PAC Rev 26 produces an average benefit of 12% and 7%, respectively. Taking the smaller benefit for each test, three of the 12 test cases produce a benefit of more than 10%. Using the 2011 version of the CMM with PAC Rev 26 produces an average benefit of 2% and 4%, respectively. Taking the smaller benefit for each test case, only two of the 12 test cases produce a benefit of more than 10%.

For test cases 13-24, the average benefit using the 2007 version of the CMM with PAC Rev 21 was 9% and 6%, respectively. Taking the smaller benefit for each test case, three of the 12 test cases produce a benefit of more than 10%. Using the 2007 version of the CMM with PAC Rev 26 produces an average benefit of 4% and 1%, respectively. Taking the smaller benefit for each test case, none of the 12 test cases produce a benefit of more than 10%. Using the 2011 version of the CMM with PAC Rev 26 produces an average benefit of 2% and 6%, respectively. Taking the smaller benefit for each test case, none of the 12 test cases produce a benefit of more than 10% and nine of the test cases show essentially no benefit at all.

These results indicate that in 2007 the benefit derived from using the HCN-based approach (using PAC Rev 21) was relatively small, but there were a significant percentage of test cases in which this approach might influence emergency preparedness planning. Using the 2011 version of the CMM with a new PAC dataset and an expanded set of HCNs, the average benefit was low and only in a small percentage of test cases would the HCN-based CMM values influence emergency preparedness planning.

Examining the data in **Tables 3** and **4** and the HCN values assigned to the chemicals in our test cases (as presented in **Appendix A**) provides clues for identifying the types of chemical mixtures that will produce the greatest benefit from using the CMM's HCN-based approach:

- If there is one chemical in a mixture that is the overwhelming contributor to the cumulative HI value (i.e., accounts for over 95% of the HI), the HCN-based approach will provide little benefit.

- If there are two or more chemicals in a mixture that are overwhelming contributors to the cumulative HI and they have an overlap in their HCN assignments (i.e., the chemicals have one or more common modes of action or target organ effects), the HCN-based approach will provide little benefit.

[a] When using the CMM's HCN-based approach, users are advised to use the largest HI value from all the mode of action and target organ effects categories to represent a maximum HI for emergency management purposes. The larger the HCN-based maximum HI value, the smaller is the benefit from using the HCN-based approach.

- If there are two or more chemicals in a mixture that are significant contributors to the cumulative HI and the chemicals do not have an overlap in their HCN assignments, the HCN-based approach should provide a benefit.

There are several of our 24 test cases in which we would expect to see a measurable benefit from using the HCN-based approach. Based on the 2011 version of the CMM with PAC Rev 26 data, Test Cases 1, 6, 23, and 24 fit the criteria for providing a likely benefit from using the HCN-based approach. In these four test cases, the average percentage benefit (taking the smaller of the mode of action and target organ benefits) is:

- 17% using the 2007 version of the CMM with PAC Rev 21
- 10% using the 2007 Version of the CMM with PAC Rev 26
- 11% using the 2011 version of the CMM with PAC Rev 26.

This amount of benefit could be significant in cases where the cumulative HI at a key receptor location has a value close to the unity (e.g., 0.9 < HI < 1.1). In other instances, a benefit of about 10% is unlikely to make a significant difference in emergency planning.

Figures 1 illustrates the significant benefits found for Test Cases 1, 6, 23, and 24 using the three different versions of the CMM used in testing. **Figure 2** illustrates the relatively insignificant benefit values, particularly using the 2011 version of the CMM, for the other 20 test cases.

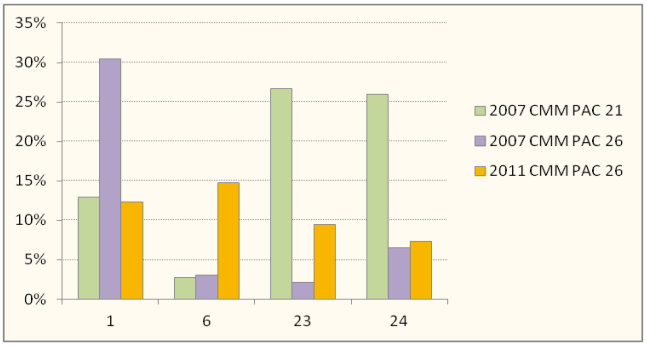

Figure 1. Benefit from using the HCN-Based Approach (%) for Test Cases 1, 6, 23, and 24.

3.4 CMM Testing Results: Differences between the Mode of Action and Target Organ Effects

Figure 3 illustrates the difference in the benefit value computed for the mode of action and the target organ effects for each of the 24 test cases. Results are presented for each of the three combinations of the CMM version and PAC revision used in our assessment. In many cases, the benefit values computed for the mode of action and target organ effects are quite similar.

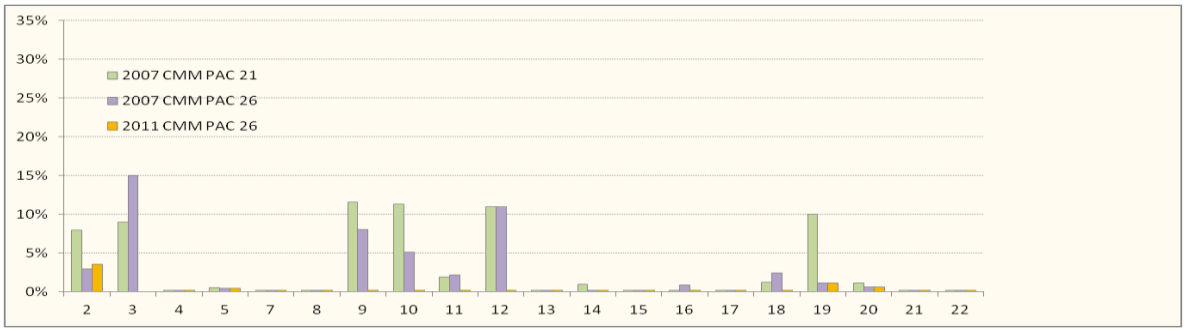

Figure 2. Benefit from using the HCN-Based Approach (%) for the Other 20 Test Cases. The benefits in these test cases are on average substantially lower than in the four test cases presented in Figure 1.

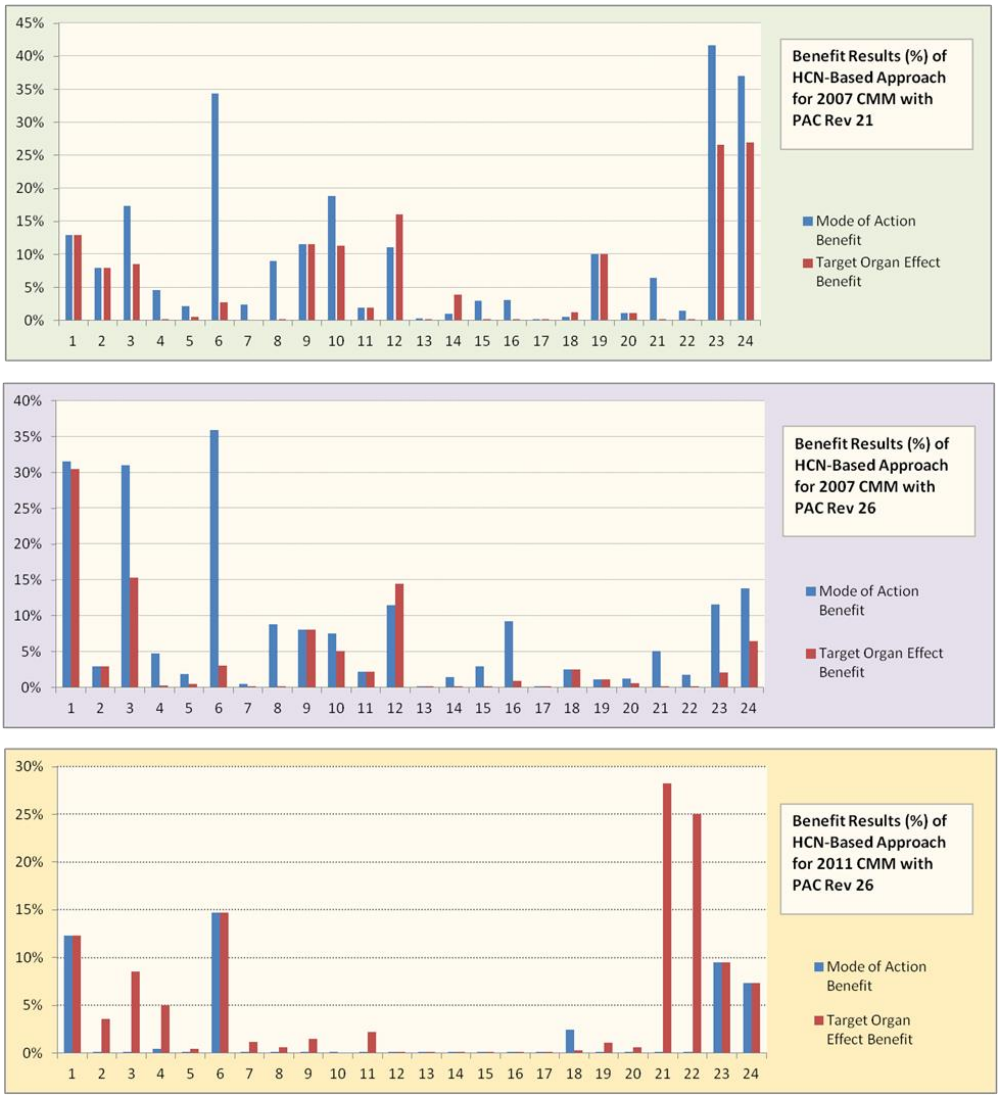

Figure 3. Benefit Calculations (%) of HCN-Based Approach Using Three Different Versions of the CMM. Results are presented for 24 test cases (along the x-axis) for the Mode of Action and the Target Organ Effect.

In other cases, there are large differences in these values. These differences may be linked to:

- The extensive use of the general HCN category "4.00" in the 2007 version of the CMM will often result in higher HI values for target organ effects than for the mode of action. This is because the HI for an HCN of "4.00" is only added in one mode of action category (i.e., *Acute System Effects*), but is added in multiple target organ categories. In contrast, a more specific "4.xy" HCN (e.g., 4.01, 4.07) is only added in a single target organ category. For example, the HI for HCN of 4.00 is added to the HIs for the HCNs of 11.00 and 11.01 to form the target organ effect for *Respiratory System Toxin and Severe and Moderate Irritants.* Similarly, the HI for an HCN of 4.00 is added to the HIs for the HCNs of 7.00, 7.01, 8.00, and 6.00 to form the target organ effect for *Nervous System Effects*. A higher cumulative HI value for the greatest target organ effect translates into a reduced benefit for the target organ effect. This accounts for the large difference in benefit values between the mode of action and the target organ effect seen in Test Cases 6 and 8 when using the 2007 version of the CMM, and the much smaller differences seen in these test cases when using the 2011 version of the CMM (where the HCN category of "4.00" is used much less frequently).

- The general HCN categories of "4.xy" and "3.xy" cover a wide range of target organ effects (e.g., *Acute Bladder Effects* [4.03], Acute Gastrointestinal Effects [4.07], Acute Bone Effects, [4.13]), yet these diverse health effects are combined into only one mode of action (i.e., *Acute System Effects*). By combining these effects, the HI for the Acute System Effects can become quite large; while the separation of these HCNs into a variety of different target organ effects can result in substantially lower HIs. This may result in larger benefits for the target organ effect than for the mode of action. Examples of this are seen in Test Cases 2 and 4 using the 2011 version of the CMM.

- The HCNs associated with severe, moderate, and mild irritation (14.xy, 14.xy, and 16.xy) form their own mode of action category but are <u>not</u> used in computing any target organ effects. For example, the eyes, nose, and skin are individual target organs; however, the HCNs associated with irritation to these organs are not considered when calculating their target organ effects (only "*acute effects other than Irritation"* are considered). As a result, in instances where the *Irritation* mode of action produces the greatest HI value, the greatest HI for a target organ effect may have a significantly lower value. It is unclear why irritation is not used to compute target organ effects to the eyes, nose, and skin. This could be changed by incorporating the generic HCNs for *Irritation* into the eye, nose, and skin target organ categories. Alternatively, although it would involve substantial effort, eye-, nose-, and skin-specific HCNs for irritation could be developed and incorporated into the corresponding eye, nose, and skin target organ categories.

- The modes of action for the *Nervous System* (7.xy) and *Reproductive System* (5.xy) combine both acute and chronic health effects. However, when considering the target organ effects of Nervous and Reproductive Systems, acute and chronic impacts are considered in separate categories. As a result, the HI calculated for the modes of action associated with these systems may be up to 50% larger than the associated target organ effect categories. Other modes of action (e.g., *Respiratory System*, *Heart*, Kidney) have separate modes of action for acute and chronic health effects so that their HIs for the mode of action and target organ effect would be similar. As a result, if the *Nervous System* or *Reproductive System* provides the highest HI value for the mode of action, the largest target organ effect may be associated with a different set of target organs and have lower HI values. This difference will show up as a larger benefit for the target organ effect than for the mode of action. This is seen in Test Cases 21 and 22 when

using the 2011 Version of the CMM (where the *Nervous System* is the dominant mode of action). This is not seen using the 2007 version of the CMM because the older HCN assignments did not explicitly identify *Nervous System*-related health effects for the key chemicals; instead, another mode of action (i.e., *Acute System Toxins*) dominates.

Some of these differences we see between the mode of action and target organ effect results may be meaningful and informative. Other differences may be an artifact of the methodology and may warrant reassessment to make the results of the CMM analysis as informative and accurate as possible.

3.5 CMM Testing Results: Modes of Action Linked to Maximum HI Values

Examining the mode of action associated with the maximum HI value for each test case provides some interesting information. Using the 2007 version of the CMM with PAC Rev 21, acute systemic toxins are the dominant mode of action in 65% of the test cases, chronic systematic toxins are dominant in 25% of the test cases, and carcinogens/mutagens are dominant in 5% of the test cases (**Figure 4**). Using the 2011 version of the CMM with PAC Rev 21, acute systemic toxins are the dominant mode of action in slightly less than 50% of the test cases, acute respiratory effects are dominant in 25% of the test cases, acute nervous system effects are dominant in 15% of the test cases, and chronic systemic toxins are only significant in 5% of the test cases (see **Figure 4**). The distribution for the 2011 CMM appears more realistic because respiratory and nervous system effects are more closely associated with a decrease in an individual's ability to take protective actions than chronic systemic effects.

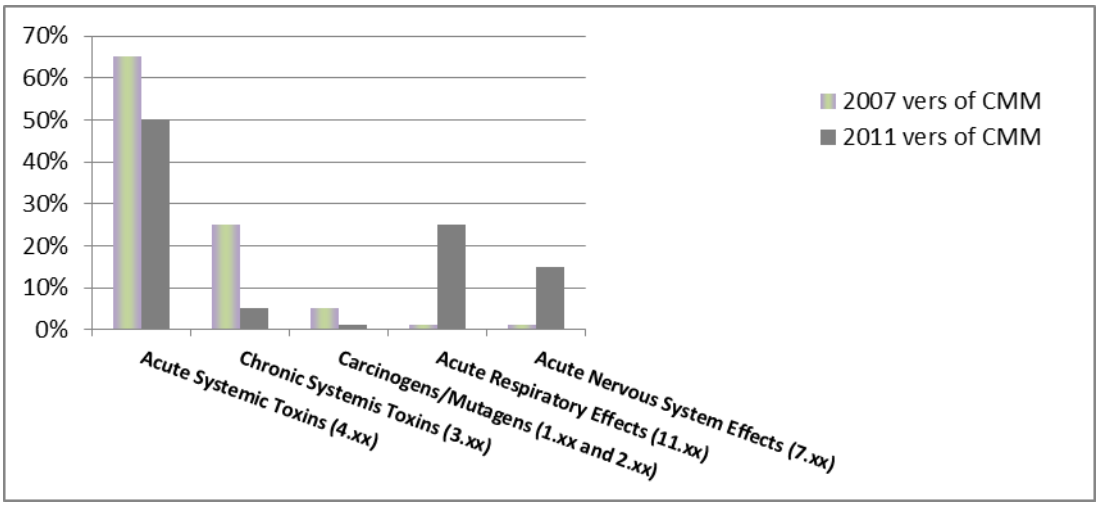

Figure 4. Modes of Action Linked to the Greatest Health Effects in 24 Test Cases.

4.0 Simple Candidate Approaches for Enhancing the CMM

This section describes simple candidate approaches for enhancing the CMM's HCN-based approach. Testing results for these candidate approaches are presented and analyzed.

4.1 Reducing Overconservatism in the CMM's HCN-Based Approach

The PAC values used in the CMM are extrapolations of potential human health impacts based on laboratory testing. The PAC values derived for a chemical may be based on only one route of exposure or impacts on a limited set of target organs that are most susceptible to the chemical. In contrast, HCNs are selected for a chemical based on whether the mode of action or a target organ can be impacted by the chemical at any concentration or duration of exposure. In other words, the current approach does not involve selecting HCNs for only the modes of action and target organs involved in the derivation of the chemical's PAC values. As a result, a chemical may have 10 HCN values assigned to it, but a PAC value for this chemical may only be linked to a small subset of these HCN values; the health effects associated with many of the HCNs linked to a chemical may only occur applicable at much higher concentrations than the PAC value.

The goal of CMM workbook's HCN-based approach is to provide a conservative estimate of the health impacts from exposure to a chemical mixture. It is intended to be conservative but to be less overly conservative than simply computing the cumulative HI for all the chemicals in the mixture. If the benefit provided by the 2011 version of the CMM's HCN-based approach is not as large as needed to effectively eliminate overconservatism, there are alternative approaches for utilizing HCN information that may provide technical defensible and less overly conservative estimates of potential health effects.

Example of an Overly-Conservative Relationship between PAC Values and HCNs

Oxalic acid dehydrate (CASRN: 6153-56-6) has a PAC-2 value of 30 mg/m^3. This PAC value is based on PEL-TWA that is designed to protect people from inhalation and skin contact with the chemical and protection from severe irritation and burning of the respiratory system, eyes, and skin. This information is appropriately captured by assigning the HCN values associated with these modes of action to this chemical. HI values calculated for these modes of action are of concern for emergency planning and response applications.

In addition to the above modes of actions, HCNs for oxalic acid dehydrate are also assigned for acute central nervous system impacts, acute gastrointestinal effects, chronic kidney impacts, and chronic heart impacts. While these modes of action are of potential concern for some routes of exposure (e.g., ingestion) and long durations of exposure, they are only of concern for emergency management purposes at concentrations much higher, and perhaps orders of magnitude higher, than captured by the PAC-2 value. As a result, application of this chemical's HI value applied to these HCN categories may be overly conservative for emergency planning and response applications.

After considering a number of potential approaches for further reducing excessive conservatism in the HCN-based approach, and discussing options with members of the chemical exposure and chemical mixtures working groups, several new HCN-based approaches have been identified. These approaches focus on easy-to-implement solutions that employ simple modifications to the CMM. In the following subsection two easy-to-implement approaches are described and the results of testing are presented. Each of these approaches makes use of weighting factors to reduce the contribution to the HIs of HCN categories that may not be of significance at the identified concentration limit (e.g., PAC-2). The use of weighting factors is not a new concept in the CMM. Currently, weighting factors of 0.5 and 0.25 are applied in the CMM for moderate and mild irritants (HCN's 15.xy and 16.xy), respectively. The approaches being tested in the current study simply extend the weighting factor concept to a broader set of HCN categories.

4.2 Approach 1 –Weighting Factors Assigned to the Top Ten HCNs for Each Chemical

Approach 1 applies a range of weighting factors to the top ten HCNs that are active for each chemical in a mixture. The weighting factors are based on the priority ranking of the HCNs assigned to each chemical (Petrocchi et al., 2008). In implementing Approach 1, a four step process is involved, with Step 1 and 2 unchanged from the current CMM implementation procedure.

1. Identify the potentially applicable HCNs for each chemical in a mixture.

2. Select the appropriate type of concentration limit data set (e.g., PAC-2)

3. Rank the top-ten HCNs for each chemical, ordered from highest to lowest health effect, according to their **effect-based rank order**. The ranking order used to support testing Approach 1 is presented in **Table 5** and is based on Petrocchi et al. (2008). In **Table 5**, the HCNs are ranked from highest to lowest impact based on the potential impairment of an individual's ability to take effective protective actions or experience irreversible or other serious health impacts (i.e., PAC-2). *Effect-based rank ordering schemes can be generated for PAC-1 and PAC-3, as can alternative schemes for PAC-2. However, **Table 5** should serve as a suitable scheme for testing purposes.*

4. Apply weighting factors to the top ten HCNs for a chemical, with the most impactful HCNs receiving a weighting factor of "1.0" and those HCNs with lower impacts receiving reduced weighting factors. A number of different weighting factor schemes were considered for use in Approach 1. Some potential candidates are listed in **Table 6**, though only testing results for *Candidate Scheme A* are presented in this report. If a moderate irritant HCN (15.xy) has a weighting factor > 0.5, reduce that weighting factor to 0.5; similarly, if a mild irritant HCN (16.xy) has a weighting factor > 0.25, reduce that weighting factor to 0.25 (these adjustments mimic what is done for moderate irritation HCNs in recent versions of the CMM).

5. Multiply the HI value for the chemical by the weighting factor for the HCN when performing HCN-based approach calculations.

Table 5. HCNs Listed in Order of Their Effect-Base Rank[4].

Rank	HCN	Target-Organ Effect
1	17.00	Asphyxiants, anoxiants—*acute effect*
2	18.00	Explosive, flammable safety (no adverse effects with good housekeeping)
3	13.00	Blood toxin, methemoglobinemia—*acute effect*
4	6.00	Cholinesterase toxin—*acute effect*
5	14.01	Eye irritant—severe
6	14.00	Severe irritant
7	15.01	Eye irritant—moderate
8	15.00	Moderate irritant
9	4.01	Eye—acute, other than irritation
10	*11.01*	*Respiratory irritant—acute severe or moderate but not mild irritant effects*
11	14.02	Skin irritant—severe
12	15.02	Skin irritant—moderate
13	4.00	Systemic toxin—acute short-term high hazard effects
14	*4.08*	*Heart, Cardiovascular system—acute effects*
15	*4.05*	*Brain—acute effects*
16	7.01	Central nervous system—acute effects
17	8.00	Narcotic—*acute effect*
18	7.00	Nervous system toxin—acute effects
19	11.00	Respiratory toxin—acute effects other than irritation
20	*4.02*	*Nose—acute effects other than irritation*
21	*4.09*	*Kidney—acute effects*
22	*4.06*	*Hematological effects—acute, unspecified*
23	*4.04*	*Bone marrow—acute blood-forming system and other acute effects*
24	*4.10*	*Liver—acute effects*
25	*4.07*	*Gastrointestinal tract—acute effects*
26	*4.03*	*Bladder—acute effects*
27	*4.13*	*Bone—acute effects*
28	3.08	Heart, Cardiovascular system—*chronic effects*
29	1.00	OSHA carcinogen (29 CFR 1910.1000)—*chronic effect*
30	1.01	Bladder carcinogen—*chronic effect*
31	1.02	Liver carcinogen—chronic effect
32	2.00	Suspect carcinogen or mutagen—*chronic effect*
33	2.01	Kidney carcinogen—*chronic effect*
34	2.02	Liver carcinogen—*chronic effect*
35	3.05	Brain—chronic effects
36	*7.11*	*Central nervous system—chronic effects*
37	*7.10*	*Nervous system toxin—chronic effects*
38	10.00	Respiratory toxin—chronic effects
39	9.00	Respiratory sensitizer—*chronic effect*
40	3.09	Kidney—chronic effects
41	3.02	Hematological effects—chronic, unspecified
42	3.04	Bone marrow—chronic blood-forming system and other chronic effects
43	3.10	Liver—chronic effects
44	3.07	Gastrointestinal tract—chronic effects
45	3.01	Bladder—chronic effects
46	3.03	Bone—chronic effects
47	3.06	Eye—chronic ocular effects
48	12.00	Blood toxin, anemia—*chronic effect*
49	5.00	Reproductive toxin—acute effects
50	*5.10*	*Reproductive toxin—chronic effects*
51	*4.11*	*Skin—acute effects other than irritation*
52	3.11	Skin—chronic effects including dermatitis and sensitization
53	*4.12*	*Skin perforation—acute effects other than skin absorption*
54	3.12	Skin perforation—nasal septum perforation and other chronic effects other than skin absorption
55	3.00	Systemic toxin—chronic effects
56	16.01	Eye irritant—mild
57	16.00	Mild irritant
58	16.02	Skin irritant—mild
59	19.00	Generally low risk health effects—nuisance particles, vapors or gases
60	20.00	Generally low risk health effects—odor

Note: HCNs additions and changes adopted since 2007 are indicted using a *blue, italicized font.*

[4] Adapted from Petrocchi et al. (2008)

Table 6. Five Weighting Factor (WF) Schemes. Candidate WF Scheme "A" is used in the testing presented in this whitepaper.

HCNs Ranking Order	Candidate A WF Scheme	Candidate B WF SCHEME	Candidate C WF SCHEME	Candidate D WF SCHEME	Candidate E WF SCHEME
1	1	1	1	1	1
2	0.9	1	1	1	1
3	0.8	0.8	0.9	1	0.75
4	0.7	0.8	0.8	0.7	0.75
5	0.6	0.6	0.7	0.7	0.5
6	0.5	0.6	0.6	0.7	0.5
7	0.4	0.4	0.5	0.7	0.5
8	0.3	0.4	0.4	0.4	0.25
9	0.2	0.2	0.3	0.4	0.25
10	0.1	0.2	0.2	0.4	0.25

In this approach, the top-ranking HCN for a chemical will receive the highest weighting factor (i.e., 1.0) regardless of where it may fall in the overall ranking of HCNs that is provided in **Table 5**. Less impactful HCNs for a given chemical will be assigned lower weighting factors.

One of the features of this approach is that it does not weight all HCNs equally. In instances where multiple HCNs are defined for a chemical, it is assumed that in most cases only a small subset of the assigned HCNs is associated with the health impacts actually seen in the laboratory studies that were used in the derivation of the chemical's PAC values. It is assumed that many of the lower-ordered HCNs may only be relevant at exposure levels much higher than indicated by the PAC values. Consequently, instead of receiving weighting factors of "1.0", as in the original HCN-based approach, these lower-ordered HCNs will receive a lower weighting factor.

A disadvantage of Approach 1 is that the ranking of the HCNs for each chemical is based on a generic ranking of health effects and not on any information about which specific mode of action or target organ was involved in determining the concentration limits for the chemical. As a result, there is no guarantee that the HCN assigned the top weighting factor will be an HCN most closely associated with the observed health effects that are used to derived the concentration limits for the chemical. Alternative weighting factor schemes can be used to assign the top weighting factor to more than one HCN. While this reduces the likelihood that the most important HCN or HCNs will be assigned a lower weighting factor, it may (like the current approach) provide weighting factors to HCNs that are too high to accurately reflect their lack of significance at the selected concentration limit.

Illustration of HCN Weighting Factors for Approach 1

The HCNs assigned to "Trimethyloctane, 2,2,6-" (CASRN: 62016-37-9) are ranked and weighted in the following manner based on Tables 5 and 6 (Scheme A):

	1	2	3	4	5
HCN:	11.01	11.00	3.05	16.01	16.02
WF:	1.0	0.9	0.8	0.25	0.25

The HCNs assigned to "uranium oxide" (CASRN: 1344-59-8) are ranked and weighted as follows:

	1	2	3	4
HCN:	2.00	3.09	3.02	3.10
WF:	1.0	0.9	0.8	0.7

4.3 Approach 2 –Weighting Factors Based on HCN Rankings for a Given PAC Level

Approach 2 applies weighting factors based on the ranking order defined for all HCNs as a function of the type of concentration limit (e.g., PAC-2). In implementing Approach 2, a three step process is involved, with Step 1 and 2 unchanged from the current CMM implementation procedure.

1. Identify the potentially applicable HCNs for each chemical in a mixture.

2. Select the appropriate type of concentration limit data set (e.g., PAC-2)

3. Rank the top-ten HCNs for each chemical based on their effect-based ranking order for the selected concentration limit. In **Tables 7** and **8**, two different weighting schemes, "Alpha" and "Beta" are presented as potential options for this approach based on their PAC-2 impact level. **Table 7** presents the "Alpha" weighting factor scheme. It uses the same ranking order as **Table 5** and assigns weighting factors of 1, 0.75, 0.5, and 0.25, with each of these four weighting factors assigned to a quarter of the HCNs in the table. **Table 8** presents the "Beta" weighting factor scheme. It places greater emphasis on acute effects and assigns weighting factors from 1.0 through 0.1 based on an alternative ranking of the HCNs for PAC-2. Additionally, under "Beta", if a given chemical does not have at least one HCN with a weighting factor of 1.0, the chemical's largest weighting factor is increased to 1.0. This ensures that at least one or more HCNs are associated with the fully weighted HI value for the chemical.

4. Multiply the HI value for the chemical by the weighting factor for the HCN when performing HCN-based approach calculations.

Table 7: Candidate WF Scheme "Alpha" Based on the Current HCN Ranking Order for PAC-2. Weighting factors of 1, 0.75, 0.5, and 0.25 are used.

Rank	HCN	WF	Rank	HCN	WF
1	17.00	1	31	1.02	0.5
2	18.00	1	32	2.00	0.5
3	13.00	1	33	2.01	0.5
4	6.00	1	34	2.02	0.5
5	14.01	1	35	3.05	0.5
6	14.00	1	36	7.11	0.5
7	15.01	0.5[a]	37	7.10	0.5
8	15.00	0.5[a]	38	10.00	0.5
9	4.01	1	39	9.00	0.5
10	11.01	1	40	3.09	0.5
11	14.02	1	41	3.02	0.5
12	15.02	0.5[a]	42	3.04	0.5
13	4.00	1	43	3.10	0.5
14	4.08	1	44	3.07	0.5
15	4.05	1	45	3.01	0.5
16	7.01	0.75	46	3.03	0.25
17	8.00	0.75	47	3.06	0.25
18	7.00	0.75	48	12.00	0.25
19	11.00	0.75	49	5.00	0.25
20	4.02	0.75	50	5.10	0.25
21	4.09	0.75	51	4.11	0.25
22	4.06	0.75	52	3.11	0.25
23	4.04	0.75	53	4.12	0.25
24	4.10	0.75	54	3.12	0.25
25	4.07	0.75	55	3.00	0.25
26	4.03	0.75	56	16.01	0.25
27	4.13	0.75	57	16.00	0.25
28	3.08	0.75	58	16.02	0.25
29	1.00	0.75	59	19.00	0.25
30	1.01	0.75	60	20.00	0.25

(a) = weighting factors for moderate irritation (15.xy) are set to 0.5, instead of 1.0, to mirror how these HCNs were weighted in recent versions of the CMM.

Table 8: Candidate WF Scheme "Beta" Based on a Revised HCN Ranking Order for PAC-2. Weighting factors ranging from 1 to 0.1 are used.

Rank	HCN	WF	Rank	HCN	WF
1	17.00	1	31	10.00	0.4
2	18.00	1	32	9.00	0.4
3	11.01	1	33	7.11	0.4
4	11.00	1	34	7.10	0.4
5	7.01	1	35	12.00	0.4
6	7.00	1	36	3.01	0.4
7	8.00	1	37	3.02	0.4
8	14.01	1	38	3.03	0.4
9	4.08	1	39	3.04	0.4
10	4.05	1	40	3.05	0.4
11	4.01	1	41	3.06	0.4
12	6.00	1	42	3.07	0.4
13	14.00	1	43	3.08	0.4
14	14.02	1	44	3.09	0.4
15	13.00	1	45	3.10	0.4
16	15.01	0.8[b]	46	3.00	0.4
17	15.00	0.8[b]	47	1.00	0.4
18	15.02	0.8[b]	48	1.01	0.4
19	4.00	0.8	49	1.02	0.4
20	4.02	0.8	50	2.00	0.4
21	4.03	0.8	51	2.01	0.4
22	4.06	0.8	52	2.02	0.4
23	4.07	0.8	53	16.01	0.2
24	4.04	0.6	54	16.00	0.2
25	4.09	0.6	55	16.02	0.2
26	4.10	0.6	56	5.10	0.2
27	4.11	0.6	57	3.11	0.2
28	4.12	0.6	58	3.12	0.2
29	4.13	0.6	59	19.00	0.1
30	5.00	0.6	60	20.00	0.1

(b) = weighting factors for moderate irritation (15.xy) are set to 0.8 in this scheme to reflect an alternative perspective on their potential impact on an individual's ability to take protective actions.

Illustration of HCN Weighting Factors for Approach 2

The HCNs assigned to "Trimethyloctane, 2,2,6-" (CASRN: 62016-37-9) are ranked and weighted in the following manner based on Tables 7 and 8.

	1	2	3	4	5
HCN:	11.01	11.00	3.05	16.01	16.02
WF- Alpha:	1.0	0.75	0.5	0.25	0.25
WF- Beta:	1.0	1.0	0.4	0.2	0.2

The HCNs assigned to "uranium oxide" (CASRN: 1344-59-8) are ranked and weighted as follows:

	1	2	3	4
HCN:	2.00	3.09	3.02	3.10
WF-Alpha:	0.5	0.5	0.5	0.5
WF-Beta:	1.0[a]	0.4	0.4	0.4

(a) = although HCN 2.00 has an assigned WF of 0.4 in Table 8, as the highest ranking HCN for this chemical, it is reassigned a WF of 1.0.

Approach 2 is a bit simpler than Approach 1, since it relies only on the generic effect-based ranking. In Approach 2, a chemical may have more than one, or even all of its HCNs assigned a top weighting factor of 1.0. If all the HCNs are assigned the top weighting factor, the contribution of that chemical towards all of the mode of action and toxic organ groupings will be same as the current, non-weighted approach. Alternatively, in Approach 2-Apha, a chemical that does not have any high ranking HCNs, may have its top HCN assigned a weighting factor that is lower, and sometime significantly lower, than 1.0. For example, in some cases, the top HCN may be assigned a weighting factor of 0.5 or less. This may provide non-conservative results in some instances, because it is assumed that the PAC-2 value is at least based on the health effects associated with one HCN category. Approach 2-Beta avoids this problem in the infrequence instances where it occurs, by always assigning the highest ranking HCN assigned to a chemical a weighting factor of 1.0, even if a lower value is specified in **Table 8**. Another interesting feature of Approach 2 is that each HCN is assigned the same weighting factor for all the chemicals in the mixture (except for instances where the highest weighting factor in Approach 2-Beta is increased to 1.0), regardless of ranking order of the HCNs assigned to each chemical.

As is the case with Approach 1, there is no guarantee that the HCN assigned the top weighting factor will be an HCN most closely associated with the projected health effects that are used to derived the concentration limits for that chemical.

4.4 Testing Results: Approaches 1 and 2

Testing of the following modified HCN-based approaches is conducted using 12 chemical mixtures:

- **Approach 1** using the priority ordering from **Table 5** and the weighting factors from **Table 6** (Scheme A)

- **Approach 2-Apha** using the weighting factors from **Table 7**

- **Approach 2-Beta** using the weighting factors from **Table 8**.

The 12 chemical mixtures used are the even-numbered test cases from the original 24 test cases presented in **Tables 1** and **2**.

In this testing, the benefit is determined by comparing results from the new approaches with the results obtained earlier for the cumulative HI values using the 2011 version of the CMM. Benefit values are determined for both the mode of action and the target organ effects. **Figures 5-10** present the results for the even-numbered Test Cases 2- 12. In assessing these results, bear in mind that the lowest of the mode of action and target organ effects benefits, represents the effective benefit for using the indicated HCN-based approach.

As we noted earlier, Test Case 6 is the only test case in this series of six tests in which we expect to see an appreciable benefit from using the standard HCN-based approach. In Test Case 6, the 2007 version of the CMM shows a benefit of 3% (based on the smaller of the mode of action and target organ effect categories) and the current 2011 version of the CMM shows a benefit of about 15%. New Approach 1 shows a benefit of 24% and new Approach 2-Alpha and 2-Beta each show benefits of about 15% (the same as the current 2011 approach).

Test Case 4 might be the most interesting of this group of test cases. Both the 2007 and standard 2011 version of the CMM provide no significant benefit. However, Approach 1, 2-Alpha, and 2-Beta all show significant benefits (22, 12, and 11%, respectively). This increase in benefit is owing to the reduced weighting applied to the HCN for A*cute Gastrointestinal Effects* (4.07), which is the lowest ranking of the 10 HCNs assigned to the two dominant chemicals in this test mixture. This reduced weighting is warranted because the Material Data Safety Sheets for the chemicals involved indicate that acute gastrointestinal effects only occur if the chemicals are ingested. In an emergency response situation, inhalation and skin irritation would be the dominant routes of exposure with ingestion being of little importance. Therefore, the new approaches are showing greater realism when they indicate that the R*espiratory System Irritant* (11.01) is the key HCN for this mixture in determining the dominant mode of action and target organ effect.

In the other four test cases (i.e., Test Cases 2, 8, 10, and 12), use of the 2007 version of the CMM with PAC Rev 21 data provides a benefit of 9 to 11% in three of the four test cases. Approach 1 provides a benefit between 12-20% in each of the four test cases. In contrast, the standard 2011 version of the CMM, Approach 2-Alpha and Approach 2-Beta indicate little or no benefit in all four test cases.

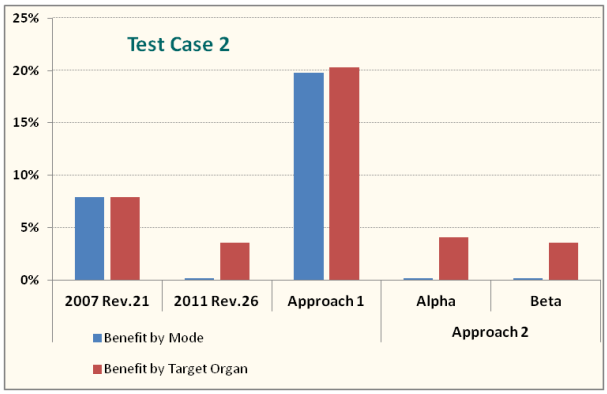

Figure 5. Results for Test Case 2

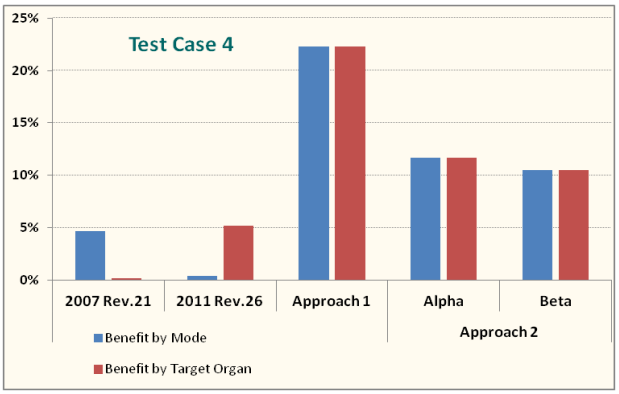

Figure 6. Results for Test Case 4

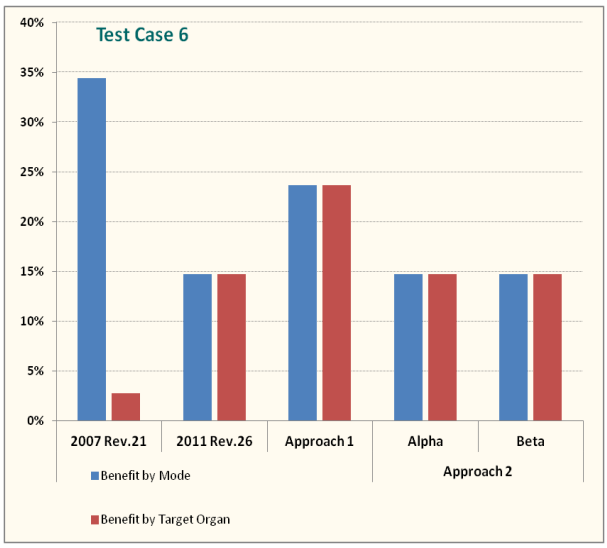

Figure 7. Results for Test Case 6

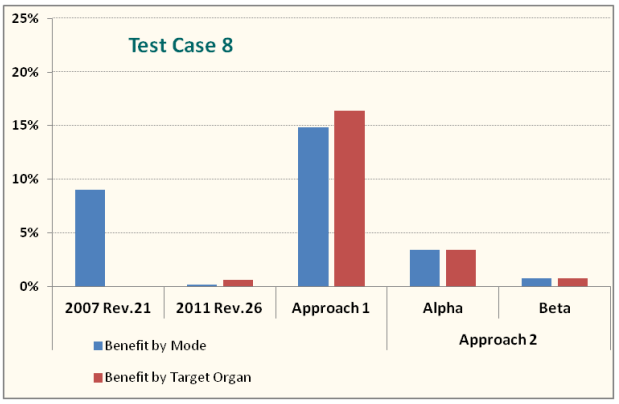

Figure 8. Results for Test Case 8

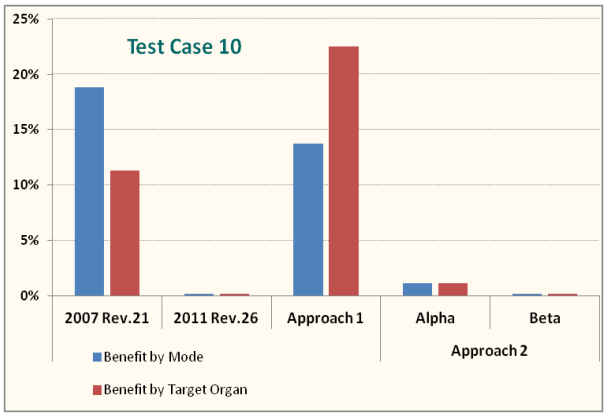

Figure 9. Results for Test Case 10

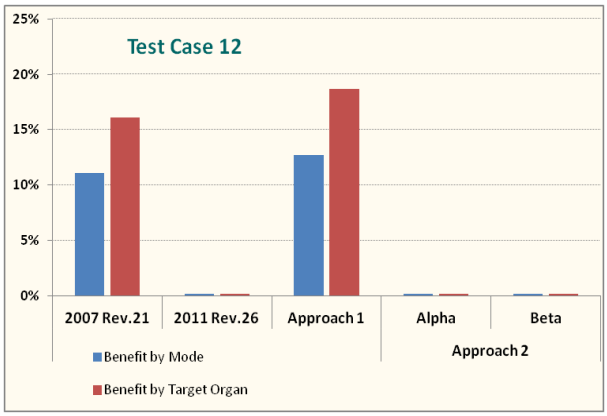

Figure 10. Results for Test Case 12

An interesting feature in these test cases is the occasional large difference observed, using a given version of the CMM, between the benefit computed for the mode of action and the benefit computed for the target organ effects. For example, in Test Case 6, the 2007 version of the CMM exhibits a huge difference between the benefit computed for the mode of action (~34%) and the benefit computed for the target organ effects (~3%). In contrast, the 2011 version of the CMM and the new approaches in Test Case 6 exhibit little if any difference between the benefit computed for the mode of action and the benefit computed for the target organ effects. This particular result can be attributed to the replacing of the generic 4.00 values in the 2007 version of the CMM with the more specific HCNs in the 2011 versions of the CMM. In all but Test Case 2, the 2007 version of the CMM exhibits appreciable differences between the benefits computed for the modes of action and the target organ effects. Appreciable differences are seen in two of the six test cases for Approach 1 and only one of test cases for the standard 2011 version of the CMM, Approach 2-Alpha and 2-Beta.

Figures 11-16 presents the results for the even-numbered Test Cases 14-24. As we noted earlier, Test Case 24 is the only test case in this series of six tests in which an appreciable benefit is seen using the standard 2011 version of the CMM.

In Test Case 24, the 2007 version of the CMM displays a benefit of 26% and the standard 2011 version of the CMM displays a benefit of about 7%. New Approach 1, 2-Alpha, and 2-Beta display a benefit of 17%, 24%, and 7%, respectively. The high benefit indicated in the 2007 version of the CMM is linked to a failure of the 2007 HCN data set to appropriately account for the respiratory irritant and respiratory toxin characteristics of the key chemicals in this mixture (this particular problem is corrected in later versions of the HCN data set). The somewhat elevated benefits for Approach 1 and 2-Alpha are linked to the questionable placement of the HCN for Moderate Eye Irritation (15.01) above the HCN for Respiratory Toxins and Irritants (11.01 and 11.00) in the traditional HCN ranking order (see **Table 5**). If the HCNs for Moderate Irritation (15.xy) are assigned a weighting factor of 0.5 in the current version of the CMM, the "15.xy" HCNs should be placed appropriately lowered on the ranking table. This is corrected in the revised HCN ranking order provided in **Table 8** and is reflected in the benefit score for Approach 2-Beta.

In Test Case 22, the 2007 version and the standard 2011 version of the CMM show no significant benefit. However, new Approach 1, 2-Alpha, and 2-Beta show benefits of 17%, 25%, and 8%, respectively. The increase in the benefit in the new approaches over the standard 2011 version of the CMM is owing to the reduced weighting factors applied to the chronic nervous system heath effects. The combination of acute and chronic nervous system effects into one *Nervous System* mode of action (as opposed to the use of separate acute and chronic modes of action as done for *Respiratory System* impacts) without some discounting of the chronic effects is responsible for the overly conservative result using the 2007 and standard 2011 versions of the CMM. The weighting factors used in the new approaches discount the chronic nervous system effects and lead to appropriately lower HI values in this *Nervous System* category. Given the characteristics of the chemicals in the other four test cases (i.e., Test Cases 14, 16, 18, and 20) little or no benefit is expected. In these four test cases, use of the standard approach with either the 2007 or 2011 version of the CMM, provides essentially no benefit (i.e., 0 to 1%). In contrast, Approach 1 provides a benefit between 2-16% in each of these four test cases, with a benefit >10% in two of these test cases. Approach 2-Alpha provides a significant benefit (22%) in one test case. Approach 2-Beta provides no significant benefit in any of these test cases.

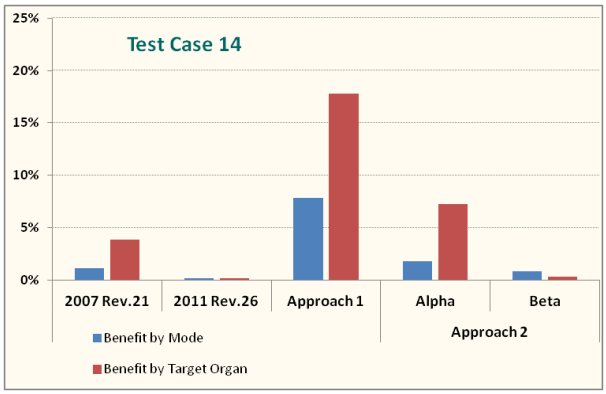

Figure 11. Results for Test Case 14

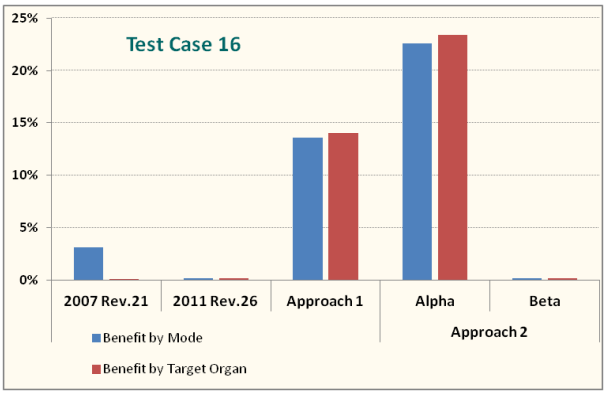

Figure 12. Results for Test Case 16

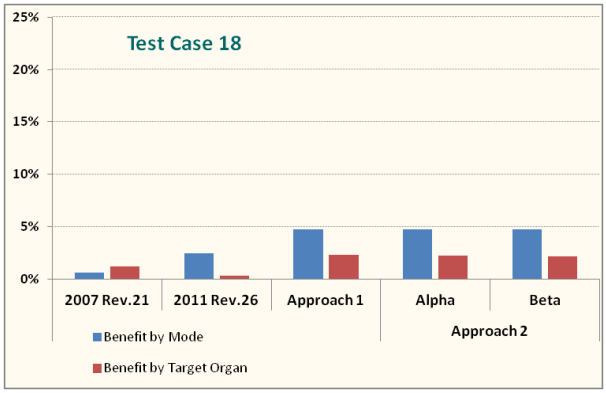

Figure 13. Results for Test Case 18

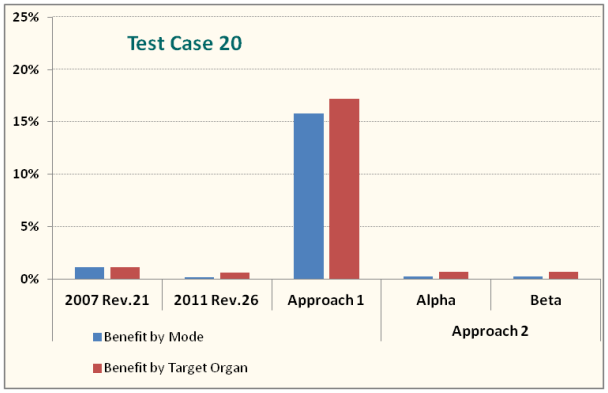

Figure 14. Results for Test Case 20

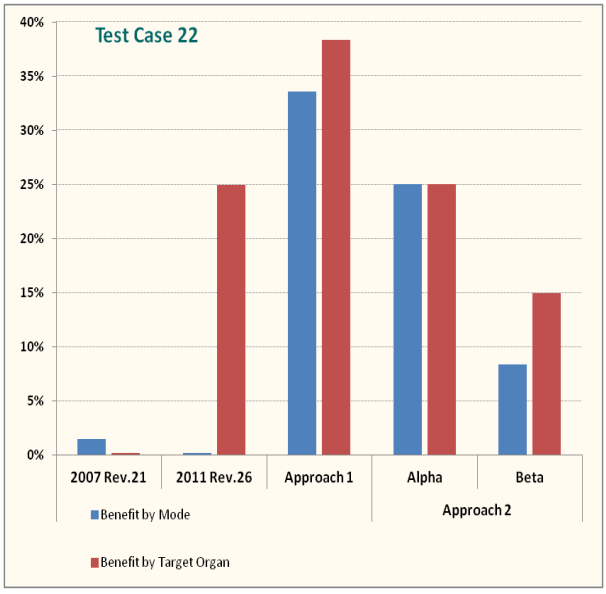

Figure 15. Results for Test Case 22

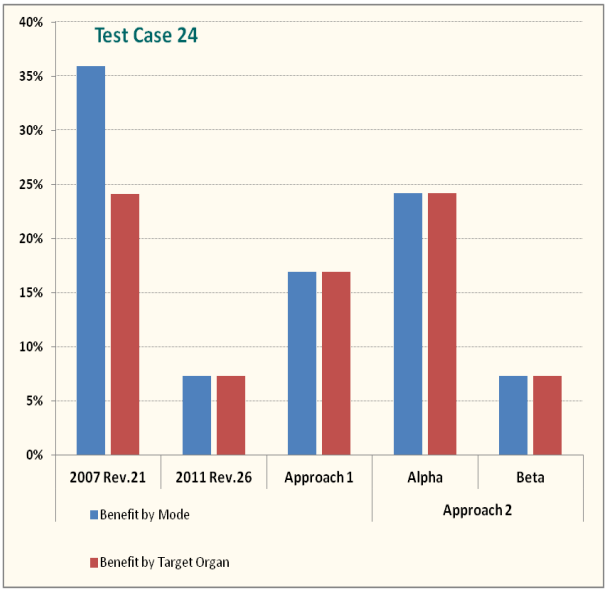

Figure 16. Results for Test Case 24

An occasional large difference is observed, using a given version of the CMM, between the benefit computed for the mode of action and the benefit computed for the target organ effects. The greatest difference is seen in Test Case 22 for using the standard 2011 version of the CMM (no benefit for the mode of action and a 25% benefit for the target organ effects). This is owing to the combination of acute and chronic nervous system effects for the mode of action and their segregation into separate categories for target organ effects. In other test cases the causes of significant differences include the lack of accounting for irritation effects for some target organs and the incorporation of multiple body systems in the mode of action category for *Acute System Effect*s.

4.5 Assessment of Approaches 1 and 2

The easy-to-implement Approaches 1 and 2 provide a benefit over the standard 2011 version of the CMM. The application of Approach 1 increases the benefit of the HCN-based approach in 11 of the 12 test cases (in Test Case 18 there is only a marginal increase in benefit). The application of Approach 2-Alpha significantly increases the benefit of the HCN-based approach in four of the 12 test cases (i.e., Test Cases 4, 16, 22 and 24). The application of Approach 2-Beta increases the benefit in only 2 of the 12 test cases (i.e., Test Cases 4 and 22).

The number of test cases with significant benefits under Approach 1 is easy to understand. In Approach 1, only one HCN category is assigned a weighting factor of "1.0", all the HCN categories are assigned somewhat lower weighting factors. As a result, the HI contribution from important health effect contributors may be reduced by 10% or more. As a result, there may be instances where the frequently application of lower weighting factors may undervalue the results in certain HCN categories and therefore underestimate the HIs for the mode of action and target organ effect. This potential under-conservatism may be eliminated through slight modifications to this approach. For example, this might involve assigning a weighting factor of 1.0 to more of the higher ranking HCN categories (e.g., using Candidate Scheme D in **Table 6**). A preliminary examination this sort of modified version of Approach 1 hint that this may produce results comparable to Approach 2-Alpha and -Beta.

The results produced by Approach 2-Alpha and Approach 2-Beta are similar in 9 of the 12 examined test cases. Significant differences, with Approach 2-Alpha producing the greater benefit, are only seen in Test Cases 16, 22, and 24. These are linked to a lower weighting factor, 0.75, used in Approach 2-Alpha for *Respiratory Toxins – Acute Effects other than Irritation* (11.00). In comparison, Approach 2-Beta uses a weighting factor of 1.0 for this HCN. This higher weighting factor seems more appropriate because it is consistent with the 1.0 weighting factor used by both versions of Approach 2 for *Respiratory Irritant – Acute Severe or Moderate Irritant Effects* (11.01).

Approach 2-Beta is the most promising of the easy-to-implement enhanced approaches to the CMM tested in this study. It provides an enhanced benefit over the standard 2011 version of the CMM in cases where such a benefit appears to be warranted. In cases where a benefit does not seem to be warranted, Approach 2-Beta provides nearly identical results as the standard 2011 version of the CMM. If further testing shows that Approach 2-Beta continues to provide appropriate and technically defensible results, while still maintaining an appropriate level of conservatism, it may prove to be a useful incremental enhancement to the HCN-based.

5.0 More Advanced Approaches for Enhancing the CMM

Approaches 1 and 2 are easy-to-implement in the short-term because they do not require changes or additions to the HCNs for the individual chemicals in the CMM workbook. Other, more advanced approaches are possible that may provide benefits that are comparable to, or greater than Approaches 1 and 2, while maintaining an appropriate level of conservatism and a higher degree of technical defensibility for all mixtures. The drawback to more advances approaches is that they may require additional work to implement. In particular, they might require additional analysis of the data used to derive the PAC/TEEL values for each chemical. Data gleamed from this analysis would be added to the CMM data set to support a more refined and chemical-specific processing of input chemical mixtures.

Two candidate advanced approaches are discussed in this section. The first of these approaches is called the **Exposure Route approach**. It involves assigning weighting factors to each chemical in a mixture based upon the route of exposure used to calculate the PAC values for each chemical. The information needed to implement this approach is readily available in the documentation used to derive the HCNs for each chemical. The second of the advanced candidate approaches is called the **Primary/Secondary/Tertiary (PST) approach**. It involves identifying the key modes of action or target organs effects observed in the studies used to derive the PAC values for each chemical. The HCNs associated with these reported health effects would be considered primary HCNs and be given a weighting factor of "1.0". The HCNs not associated with the observed health effects would be considered secondary or tertiary HCNs and assigned lower weighting factors. It is assumed that these HCNs, if not associated with the health effects observed at the PAC concentration limit, could only produce health effects at concentrations greater, or perhaps much greater, than the PAC value. This approach would require a careful review of the literature used to indentify applicable HCN values for the each chemical in the CMM data set.

In the following sections the Exposure Route and PST approaches are discussed in more detail.

5.1 The Exposure Route Approach

To implement the exposure route approach, a seven step process is involved, with Step 1 and 2 unchanged from the current CMM implementation procedure:

1. Identify the potentially applicable HCNs for each chemical in the mixture.

2. Select the appropriate type of concentration limit data set (e.g., PAC-2).

3. Rank the top-ten HCNs for each chemical based on their effect-based ranking order. The selection of the top-ten HCs may be based on the rankings provided in **Tables 7** or **8** for PAC-2, or an alternative table developed for PAC-1, -2, or -3.

4. For each chemical in the mixture, apply an initial weighting factor to the top ten HCNs. This initial weighting factor is based on the routes of exposure used in the studies that were used to derive the PAC values for the chemical. **Figure 17** displays the priority order of the references used to identify the routes of exposure for each chemical. If the relevant studies involve inhalation, skin contact, or eye contact as the primary route of exposure, initial weighting factors of 1.0 are assigned to all of the top-ten

HCNs that may involve these routes of exposure. If other routes of exposure are involved (e.g., oral, intravenous) the appropriate weighting factor from **Figure 18** is assigned to the HCN. If multiple routes of exposure are indicated, the highest applicable weighting factor is used.

5. If none of the HCNs has an initial weighting factor of 1.0, substitute 1.0 for the highest-listed weighting factor for the chemical.

6. Apply an additional weighting factor to each HCN. For PAC-2, this may involve the use of the weighting factors presented in **Tables 7** or **8**.

7. Multiple the initial and additional weighting factors together to get a final weighting factor for all of the top-ten HCNs for this chemical. Multiply the HI value for the chemical by the final weighting factor when performing HCN-based approach calculations.

Order	References
1	AGEL: human data under acute exposure
2	ERPG: human toxicity data under acute exposure
3	HSDB: acute toxicity under acute exposure
4	RTECS: acute toxicity data
5	NIOSH: safety cards and pocket guide
6	CHRIS: symptom following exposure
7	SAX11: safety profile
8	MSDS, e.g., Sigma-Aldrich

Figure 17. Order of References to Consult When Deriving Initial Weighting Factors for Each Chemical[5]

[5] The references are in the same priority order as recommended in the HCN development procedure by Petrocchi et al. (2008).

Exposure Routes	Initial WF
inhalation	1.0
skin and /or eye contact	1.0
oral	0.75
other routes	0.5
non-primary target organ or mode of action	0.25

Figure 18. Initial Weighting Factors for the Exposure Route Approach

The Exposure Route approach has not been fully tested. Several preliminary tests have been run to evaluate the routes of exposure for selected chemicals. This testing was done using the literature originally used to derive the chemical's current HCN values. The focus of this testing was to assess the correlation between HCNs and routes of exposures and assess the use of weighting factors (like those shown in **Figure 18)**. Additional testing is needed to address the viability of this approach.

Consideration of the relevance of the exposure routes for various PACs may provide food for thought for the PAC development team. The PAC team may wish to consider the relevance of the exposure route in the PAC derivation process.

Example Application of the Exposure Route Approach

Consider a mixture containing oxalic acid dehydrate (CASRN: 6153-56-6). PAC-2 values are being used in this CMM analysis and oxalic acid dehydrate has a PAC-2 value of 30 mg/m^3. This PAC value is based on PEL-TWA which was derived through experiments involving the skin/eyes and oral pathways. First the HCNs are ranked according to their order in **Table 8**. The initial weighting factor (see **Figure 18)** of 1.0 is set for HCNs with an inhalation, skin, or eye exposure route and 0.75 is set for those with an oral exposure route. Next, an additional weighting factor is applied to all HCNs using the PAC-2 weighting factors from **Table 8**. The final weighting factors represent the product of the initial and additional weighting factors and it is these final weighting factors which are used in the CMM analysis.

	1	2	3	4	5	6	7	8	9	10
HCN:	**11.01**	**11.00**	**7.01**	**14.01**	**4.01**	**15.02**	**4.07**	**4.11**	**3.08**	**3.09**
Initial WF:	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**	**0.75**	**1.0**	**0.75**	**0.75**
Add. WF:	**1.0**	**1.0**	**1.0**	**1.0**	**1.0**	**0.8**	**0.8**	**0.6**	**0.4**	**0.4**
	1.0	**1.0**	**1.0**	**1.0**	**1.0**	**0.8**	**0.6**	**0.6**	**0.3**	**0.3**

5.2 The Primary/Secondary/Tertiary (PST) Approach

The PST approach is based on the principle that the concentration limit for a chemical is typically based on a small number (or just one) of the observed modes of action or target organ effects. In this approach, only those HCNs associated with derivation of the PAC-2 are defined as primary HCNs and would be assigned a weighting factor of 1.0. Other HCNs would be assigned appropriately lower weighting factor values that reflect their health effects only showing up at higher concentration levels than PAC-2 concentration. Secondary HCNs are those associated with health effects that are listed in the literature as clearly observed during testing but are secondary in importance to the primary health effects observed at the tested concentrations. Tertiary HCNs are those associated with health effects that are of minor importance or toxic effects that did not show during the studies used to define PAC value (e.g., health effects associated with concentrations much greater than the PAC value).

To use the PST approach, information is needed on the health effects that are observed during the studies that are used to derive the PAC values for each chemical.

To implement the PST approach, a six step process is involved, with Step 1 and 2 unchanged from the current CMM implementation procedure:

1. Identify the potentially applicable HCNs for each chemical in the mixture.

2. Select the appropriate type of concentration limit data set (e.g., PAC-2).

3. Rank the top-ten HCNs for each chemical based on their effect-based ranking order. The selection of the top-ten HCs may be based on the rankings provided in **Tables 7** or **8** for PAC-2, or an alternative table developed for PAC-1, -2, or -3.

4. For each chemical in the mixture, identify the health effects observed in the studies used to derive the selected PAC value for the chemical. Determine which HCNs are associated with this observed health effect – these are the "primary" HCNs. Assign the primary HCNs a weighting factor of "1.0". All other HCNs are now considered "secondary" or "tertiary" HCNs.

5. Apply weighting factors to the secondary and tertiary HCNs for the chemical using the weighting factors obtained from **Tables 7** or **8** for PAC-2, or another accepted alternative. A secondary or tertiary HCN cannot be assigned a weighting factor of 1.0. If a weighting factor of 1.0 is listed in the selected table for a secondary HCN, reduce the weighting factor to "0.9". If a weighting factor of greater than 0.5 is listed in the selected table for a tertiary HCN, reduce the weighting factor to 0.5.

6. Multiply the HI value for the chemical by the weighting factor for the HCN when performing HCN-based approach calculations.

While requiring a more intensive analysis of the technical literature (i.e., to relate the PAC and HCN assignments for each chemical) than the other alternatives, the PST approach might be the most accurate while still maintaining an appropriate level of conservatism. Because weighting factors of 1.0 are applied to all of the HCNs that produce health effects in studies used to derive the PAC value, this approach should not produce a non-conservative result. This approach may provide the greatest level of technical defensibility of the approaches presented in this paper, though it would require the most amount of work

to implement. In addition to the more in-depth literature review, this approach would require modifications to our HCN development procedure.

Example Application of the Primary/Secondary Assessment Approach

Consider a mixture containing oxalic acid dehydrate (CASRN: 6153-56-6). PAC-2 values are being used in this CMM analysis and oxalic acid dehydrate has a PAC-2 value of 30 mg/m^3. This PAC value is based on PEL-TWA which was derived through experiments involving the skin/eyes and oral pathways. The primary health effects observed in these experiments involve severe irritation and burns to nose, eyes, throat, and respiratory tract. The HCNs associated with these health effects are assigned a weighting factor of 1.0. Secondary health effects observed includes impacts to the kidney and brain. All of the HCNs not associated with primary health effects are assigned weighting factors from **Table 8**. Those non-primary HCNs with a weighting factor of 1.0 in **Table** 8, have their weighting factors reduced to 0.9.

HCN:	**11.01**	**7.01**	**11.00**	**15.02**	**4.11**	**14.01**	**4.01**	**4.07**	**3.09**	**3.08**
WF:	**1.0**	**0.9**	**1.0**	**0.8**	**0.6**	**1.0**	**0.9**	**0.8**	**0.4**	**0.4**

6.0 Conclusions and Recommendations

The performance of the CMM has improved over the past few years as a result of three factors:

1. continuing improvement in the PAC data used to calculate HIs;

2. adoption of new HCNs to effectively capture the acute health effects that are of paramount importance in emergency planning and response;

3. marked improvement in the assignment of HCNs for the over 3,300 chemicals in the CMM data set.

A series of 24 sets of chemical mixtures were used to assess the performance of the CMM. The first phase of this assessment examined whether changes in PAC values between PAC Revs 21 and 26 had big impacts on the cumulative HI values calculated for the test mixtures. Because the HI is inversely proportional to the applicable concentration limit, large changes in a PAC value for a given chemical would be associated with large changes in the HI for that chemical. The PAC values used in our testing did not show a significant upward or downward change in the average PAC value between PAC Rev 21 and 26. However, significant changes (as much as several orders of magnitude) were seen in the individual PAC values used in our test mixtures. This caused significant upward and downward changes in the chemical-specific HIs and the cumulative HIs between the 2007 version of the CMM with PAC Rev 21 and the 2011 version of the CMM with PAC Rev 26.

Next, the benefit of using the HCN-based was evaluated. In the 24 test cases, the 2007 version of the CMM with PAC Rev 21 produced an average benefit of about 11%, with 7 of 24 test cases exhibiting a benefit > 10%. The 2007 version of the CMM with PAC Rev 26 produced an average benefit of about 8%, with 3 of 24 test cases producing a benefit > 10%. Finally, the 2011 version of the CMM with PAC Rev 26 produced an average benefit of about 4%, with only 2 of 24 test cases having a benefit > 10%.

The decrease in the benefit of the HCN-based approach from 2007 to 2011 was initially a concern, but a careful assessment of the data indicated that the current version of the CMM is more accurate than the older version of the CMM. The introduction of new HCN categories and the better characterization of HCNs for all the chemicals in the CMM data set have improved the CMM. In some cases these changes have acted to increase the benefit in from using the HCN-based approach and in other cases these changes have acted to decrease the benefit.

The HCN-based approach is not designed to provide benefits over the cumulative HI calculation for many types of mixtures. No benefit should be seen when there is only one chemical in mixture that is an overwhelming contributor to the cumulative HI value (i.e., accounts for over 95% of the HI) and when there two or more chemicals in a mixture that are overwhelming contributors to the cumulative HI and they have an overlap in their HCN assignments (i.e., the chemicals have one or more common modes of action or target organ effects). However, the HCN-based approach should provide significant benefits when there are two or more chemicals in a mixture that are significant contributors to the cumulative HI and the chemicals do not have an overlap in their HCN assignments.

In assessing the HCN-based approach, the current method was found to be overly conservative in a number of instances. There are several enhancements to the current HCN characterization and

categorization that should be considered to reduce over-conservatism and improve accuracy. These include:

- continuing to replace generic 3.00 and 4.00 HCNs with more specific values

- breaking up mode of action categories that may be overly broad (e.g., acute system effects, chronic system effects). This may be accomplished by splitting the HCNs that make up an extremely broad category into two or more categories.

- separating acute and chronic target organ effects into separate categories. Currently this is done for some but not all target organs.

- including the impact of the HCNs for severe and moderate irritation when estimating target organ effects. For example, the HCNs for irritation to the eyes, nose, and skin are currently ignored when considering the target organ effects for these organs. In contrast, irritation to the respiratory system is explicitly considered when calculating acute respiratory effects. The explicit consideration of irritation can be accomplished by creating new HCNs for the irritation to susceptible target organs, or by including the current, generic irritation HCNs when formulating certain target organ effects.

It is recommended that the Chemical Mixture working group discuss consider these ideas before planning the implementation of the next major revision to the CMM (e.g., Rev 27a or 28).

The concentration limits used in the CMM (e.g., PAC-2 values) are based on studies in which only a small subset of the HCNs identified for a chemical might be associated with observed health effects at the identified concentration limit. Health effects associated with the other HCNs might only be observed at much higher chemical concentrations. In the current HCN-based approach, up to 10 HCNs are identified for each chemical and each HCN is given full weight in determining HI values for each applicable mode of action and target organ effect. This equal weighting is likely to be over-conservative and in some cases extremely over-conservative. The challenge in reducing this over-conservatism is to identify, for each chemical, the HCNs that deserve full weighting at the concentration limit and those HCNs that should be given a lower weighting because they could not cause a health effect at the concentration limit.

Several easy-to-implement approaches to address this challenge have been developed and then tested using 12 sets of chemical mixtures. These approaches all involve different methods of prioritizing and weighting the HCNs assigned to each chemical. One thing these methods have in common is they provide higher ranking to acute effects and lower ranking to chronic effects. This makes a lot of sense from an emergency management perspective. However, chronic effects cannot be totally discounted because some concentration limits consider "irreversible or other serious, long-lasting, adverse health effects" which may not impair a person's short-term ability to take protective actions.

All of the tested, easy-to-implement approaches provided an average increase in benefit over the current version of the CMM. However, Approach 1 appears to provide more benefit than warranted by the properties of the chemicals in the mixtures. A change in the weighting scheme used by Approach 1 might correct this problem. Approach 2-Alpha and Approach 2-Beta are more conservative than the tested version of Approach 1, with Approach 2-Beta providing the more appropriate level of conservatism. Small but significant benefits are observed using Approach 2-Beta when conditions are appropriate for benefits to be experienced. The downside to these new approaches is that without detailed

information on which HCNs produced health effects at the chemical's concentration limit, these new approaches may, for some chemicals, apply too small a weighting factor to one or more of the applicable HCNs. On the plus side, Approach 1, 2-Alpha, and 2-Beta would all be easy to implement because they require no changes to the CMM data set, only the application of already available information in calculating the HIs for a mixtures mode of action and target organ effect .

In addition to the easy-to-implement approaches, two more advanced approaches have been identified. These are the Exposure Route and the PST approaches. Neither of these approaches has been fully tested. The Exposure Route approach uses weighting factors based on the exposure route used in the studies involved in the derivation of the concentration limit. It also applies a second weighting factor to each chemical's HCNs, following a rank ordering as used in Approach 2. The exposure route data required to implement this approach is relatively easy to acquire and factor into the CMM calculations.

The PST approach is the most attractive from a technical standpoint because it prioritizes the HCNs based on their likely contribution to the health effects observed in the studies used to derive the concentration limits. The implementation of this approach would require the most amount of work because it would involve reviewing the data that was assessed to identify the applicable HCNs for each chemical. On the plus side, the PST approach would maintain an appropriate level of conservatism and the highest level of technical defensiveness of any HCN-based approach.

As a next step in the process of improving the CMM's HCN-based approach, the following recommendations are proposed:

- Additional testing should be conducted on easy-to-implement enhancements to the CMM's HCN-based approach. The objective would be to identify and thoroughly assess a method for implementing HCN weighting factors that could serve as a near-term option for enhancing the performance of the CMM's HCN-based approach.
- Initial testing should be conducted by the CMM program's research interns on the proposed Exposure Route and PST approaches. The goal would be to gauge the benefit of these approaches and clearly ascertain the level of effort that would be required to gather the information needed to fully implement one of these two long-term approaches.
- NA-41 and the Chemical Mixtures working group should discuss the results of the next phase of testing and, if warranted, develop a plan and schedule for implementing cost-effective enhancements to the CMM's HCN-based approach. Through the use of national laboratory research interns, many enhancements to the current approach should be implementable at a minimal cost to the CMM program.

7.0 References

Craig, D.K., A.J. Petrocchi, C.S. Glantz, X.Y. Yu, J.A. Bond, P.R. Bouslaugh, H. he, and K.A. Schutte. *The User's Guide for the Chemical Mixture Methodology (Compatible with PAC Rev. 26, February 2011)*. 2011. PNNL-SA-76932, PNNL, Richland, WA.

Minino, AM and BL Smith. 2001. *Deaths: Preliminary Data for 2000*. National Vital Statistics Reports – Volume 49, Number 12. National Center for Health Statistics, Centers for Disease Control and Prevention, US Department of Health and Human Services.

Petrocchi, AJ; DK Craig; JA Bond; DM Trott; and XY Yu. 2008. *"Health Code Number (HCN) Development Procedure".* URS-WD Report 28008-2009.03-A

Yu, X.Y., R. Petrocchi, D.K. Craig, C.S. Glantz, D.M. Trott, J.T. Ciolek, P.Y. Lu, J.A. Bond, T.E. Tuccinardi, and P.R/ Bouslaugh. 2010. *"The Development and Application of the Chemical Mixture Methodology in Analysis of Potential Health Impacts from Airborne Release in Emergencies."* Journal of Applied Toxicology, Volume 30, issue 6 pages 513-524. August 2010. (PNNL-SA-72418, Pacific Northwest National Laboratory, Richland, WA.)

Appendix A. Test Case HCN Data

This appendix presents the chemical and HCN Data used in each of the 24 test cases. HCN data are presented for the 2007 version of the CMM and the 2011 version of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Calcium chloride dihydrate	10035-04-8	500	**7.00E-3**	19.00										3
2	Carbon; (Graphite, synthetic)	7440-44-0	10	**8.75E-1**	4.00	5.00	16.00	10.00							1B
3	Sodium oxalate	62-76-0	50	**3.50E-2**	4.00	7.01	3.08	3.09							4
4	Sodium metabisulfite	7681-57-4	25	**7.00E-2**	4.00	5.00									4
5	Sodium bromide	7647-15-6	35	**5.00E-2**	5.00	4.00	3.06	3.02	7.00						4
6	Magnesium carbonate; (Magnesite)	546-93-0	50	**1.59E-1**	19.00	10.00									1C
7	Zinc acetate	557-34-6	6	**2.92E-1**	4.00	5.00									2
8	Ammonium thiocyanate	1762-95-4	200	**8.75E-3**	4.00	7.01									2
9	Sodium phosphate, tribasic	7601-54-9	500	**3.50E-3**	4.00	14.00									1B
10	Sulfur	7704-34-9	2.5	**6.36E-1**	4.00	15.01									1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Calcium chloride dihydrate	10035-04-8	500	**7.00E-3**	14.01	4.01	3.03	5.00	5.10						1B
2	Carbon; (Graphite, synthetic)	7440-44-0	10	**8.75E-1**	15.01	11.01	4.07	4.08	5.00	3.08					1B
3	Sodium oxalate	62-76-0	6	**2.92E-1**	15.01	15.02	4.08	4.05	7.00	11.00	4.09	4.07			1B
4	Sodium metabisulfite	7681-57-4	25	**7.00E-2**	15.01	11.01	15.02	4.08	11.00	4.02	4.07	3.05	9.00	3.09	1B
5	Sodium bromide	7647-15-6	35	**5.00E-2**	15.01	4.01	4.05	7.01	7.00	4.06	3.05	7.11	7.10	3.09	1B
6	Magnesium carbonate; (Magnesite)	546-93-0	200	**3.97E-2**	15.01	15.02	11.01	10.00	4.08	4.10	4.09	4.06	3.07		1B
7	Zinc acetate	557-34-6	6	**2.92E-1**	15.01	11.01	4.08	4.06	4.07	4.10	3.02	3.10	5.00	5.10	1B
8	Ammonium thiocyanate	1762-95-4	200	**8.75E-3**	15.01	11.01	4.05	7.01	7.00	4.10	4.07	12.00	3.12		1B
9	Sodium phosphate, tribasic	7601-54-9	500	**3.50E-3**	14.01	4.01	11.01	14.02	11.00	4.07	4.05	7.01			1B
10	Sulfur	7704-34-9	30	**5.30E-2**	14.01	4.01	11.01	4.08	11.00	4.07	14.02	7.01	4.09	10.00	1B

Figure A.2. Chemical and HCN Data for Test Case 2: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Silica, crystalline-quartz; (Silicon dioxide)	14808-60-7	0.3	2.12E+1	2.00	4.00	10.00								4
2	Lithium bromide	7550-35-8	15	1.52E+0	4.00	8.00	3.11	7.01							4
3	Sodium chloride	7647-14-5	300	3.50E-2	4.00	5.00	3.02	15.01	16.02						1B
4	Sodium phosphate, tribasic	7601-54-9	500	3.50E-3	4.00	14.00									1B
5	Sulfuric acid	7664-93-9	8.7	2.38E+0	2.00	4.00	14.00	10.00	5.00						1A
6	Hydrogen chloride; (Hydrochloric acid)	7647-01-0	32.8	1.45E+0	4.00	14.01	14.02	5.00	11.00						1A
7	Phosphoric acid	7664-38-2	500	2.83E-2	4.00	14.01	14.02								1A
8	Hexane	110-54-3	11600	7.96E-4	4.00	7.01	7.00	5.00	8.00						4
9	Phthalic acid	88-99-3	0.5	3.50E+0	15.00	11.00	12.00	3.02							1B
10	Mercury vapor	7439-97-6	1.7	1.02E+1	7.01	3.07	2.00								4
11	Iron	7439-89-6	30	2.12E-1	4.00	12.00	10.00	3.10	7.00						4
12	Sodium sulfite	7757-83-7	50	3.50E-2	4.00										4
13	Methylene chloride	75-09-2	1940	9.55E-3	17.00	3.10	7.01	14.00	5.00						4
14	Sodium bromide	7647-15-6	35	2.50E-1	5.00	4.00	3.06	3.02	7.00						4
15	Hydroxylamine chloride; (Hydroxylamine hydrochloride)	5470-11-1	60	5.83E-2	4.00										2

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Silica, crystalline-quartz; (Silicon dioxide)	14808-60-7	2	3.17E+0	15.01	11.01	11.00	4.10	4.07	2.00	10.00	3.02			1B
2	Lithium bromide	7550-35-8	15	1.52E+0	7.01	7.00	4.11	4.08	4.06						4
3	Sodium chloride	7647-14-5	300	3.50E-2	15.01	4.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	4.09	1B
4	Sodium phosphate, tribasic	7601-54-9	500	3.50E-3	14.01	4.01	11.01	14.02	11.00	4.07	4.05	7.01			1B
5	Sulfuric acid	7664-93-9	8.7	2.38E+0	2.00	15.02	14.01	10.00	11.01	4.07	4.08	11.00			1A
6	Hydrogen chloride; (Hydrochloric acid)	7647-01-0	32.8	1.45E+0	6.00	14.01	4.01	11.01	14.02	4.08	7.00	11.00	4.02	4.09	1A
7	Phosphoric acid	7664-38-2	500	2.83E-2	11.01	14.01	14.02	4.08	7.01	11.00	4.10	4.07			1A
8	Hexane	110-54-3	11600	7.96E-4	17.00	14.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	1B
9	Phthalic acid	88-99-3	0.5	3.50E+0	15.01	11.01	15.02	8.00	7.01	7.00	11.00	4.07	3.09	3.02	1B
10	Mercury vapor	7439-97-6	1.7	1.02E+1	11.01	4.08	4.05	7.01	7.00	11.00	4.09	4.10	4.07	3.08	1B
11	Iron	7439-89-6	40	1.59E-1	4.01	4.08	4.10	4.07	3.08	10.00	3.10	12.00	5.10		4
12	Sodium sulfite	7757-83-7	20	8.75E-2	4.08	4.05	7.01	8.00	7.00	11.00	4.04	4.07	10.00	4.11	4
13	Methylene chloride	75-09-2	1940	9.55E-3	13.00	15.01	4.01	11.01	14.02	4.08	4.05	7.01	8.00	7.00	1A
14	Sodium bromide	7647-15-6	35	2.50E-1	15.01	4.01	4.05	7.01	7.00	4.06	3.05	7.11	7.10	3.09	1B
15	Hydroxylamine chloride; (Hydroxylamine hydrochloride)	5470-11-1	60	5.83E-2	15.01	11.01	15.02	4.05	7.01	4.07	4.06				1B

Figure A.3. Chemical and HCN Data for Test Case 1: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Cyclopropane	75-19-4	6000	**2.92E-4**	8.00	5.00	3.08	17.00	7.00						4
2	Iron(II) chloride tetrahydrate	13478-10-9	7.5	**2.33E+0**	4.00	16.00									1B
3	Ethylene oxide; (Oxirane)	75-21-8	81	**1.96E-1**	15.00	10.00	3.00	7.00	2.00						4
4	Acrylic acid polymers; (Acrylic polymer or resin)	9003-01-4	200	**1.75E-2**	4.00										2
5	Iron	7439-89-6	30	**5.83E-1**	4.00	12.00	10.00	3.10	7.00						4
6	Potassium chloride	7447-40-7	15	**1.17E+0**	4.00	3.02	3.08	16.01							1B
7	Sodium perrhenate; (Rhenium(VII) sodium	13472-33-8	50	**3.50E-3**	4.00	3.00									4
8	Palladium	7440-05-3	50	**3.50E-3**	3.11	11.00	5.00	3.02	3.04						4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Cyclopropane	75-19-4	6000	**2.92E-4**	4.01	11.01	4.08	7.01	8.00	7.00	11.00	4.07	3.08	5.00	1B
2	Iron(II) chloride tetrahydrate	13478-10-9	7.5	**2.33E+0**	14.01	11.01	14.02	4.07							1B
3	Ethylene oxide; (Oxirane)	75-21-8	81	**1.96E-1**	15.01	4.01	15.02	4.05	7.01	8.00	7.00	11.00	4.02	4.09	1A
4	Acrylic acid polymers; (Acrylic polymer or resin)	9003-01-4	200	**1.75E-2**	15.01	11.01	15.02								1B
5	Iron	7439-89-6	40	**4.38E-1**	4.01	4.08	4.10	4.07	3.08	10.00	3.10	12.00	5.10		4
6	Potassium chloride	7447-40-7	15	**1.17E+0**	15.01	11.01	4.05	4.08	7.01	7.00	11.00	4.09	4.06	4.07	1B
7	Sodium perrhenate; (Rhenium(VII) sodium	13472-33-8	150	**1.17E-3**	4.08	7.00	11.00								2
8	Palladium	7440-05-3	20	**8.75E-3**	11.01	8.00	11.00	4.07	10.00	9.00	3.09	3.02	3.04	5.10	1B

Figure A.4. Chemical and HCN Data for Test Case 4: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.00	11.00	2.00	5.00	4.00						1B
2	Citric acid	77-92-9	250	**3.50E-2**	4.00	14.01	15.02								1B
3	Agar	9002-18-0	500	**7.00E-3**	3.07										3
4	Boric acid	10043-35-3	100	**5.25E-2**	4.00	3.11	3.07	5.00	16.01						1B
5	Magnesium chloride	7786-30-3	50	**1.14E-1**	4.00	3.11									2
6	Potassium chloride	7447-40-7	15	**4.08E-1**	4.00	3.02	3.08	16.01							1B
7	Sodium carbonate	497-19-8	50	**1.75E-1**	4.00	5.00	15.01	16.02							1B
8	Sodium phosphate, tribasic; (Sodium hexametaphosphate; Calgon)	10124-56-8	500	**3.50E-3**	14.01	3.11									1B
9	Sodium hydroxide	1310-73-2	5	**3.50E-1**	4.00	14.01	14.02								1A
10	Sodium bicarbonate	144-55-8	50	**9.80E-3**	4.00	5.00	3.09	11.00	16.00						1B
11	Lithium hydroxide	1310-65-2	1	**3.50E-1**	4.00	14.00	7.01								1B
12	Potassium ferricyanide	13746-66-2	30	**1.17E-2**	4.00										2
13	Manganese(II) chloride (1:2); (Manganous chloride)	7773-01-5	11.5	**3.04E-2**	5.00	7.00	10.00								4
14	Molybdenum trioxide	1313-27-5	7.5	**4.67E-2**	2.00	16.00	4.00	11.00	3.00						1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.01	11.01	14.02	4.08	7.01	8.00	11.00	4.07	2.00	2.02	1B
2	Citric acid	77-92-9	125	**7.00E-2**	14.01	4.01	11.01	15.02	4.08	4.05	11.00	4.06	4.10	4.07	1B
3	Agar	9002-18-0	500	**7.00E-3**	3.07	4.07									4
4	Boric acid	10043-35-3	150	**3.50E-2**	4.01	11.01	4.08	4.05	7.01	8.00	7.00	11.00	4.09	4.07	1B
5	Magnesium chloride	7786-30-3	300	**1.90E-2**	11.01	4.08	4.05	7.01	8.00	7.00	11.00	4.01	4.06	7.10	1B
6	Potassium chloride	7447-40-7	15	**4.08E-1**	15.01	11.01	4.05	4.08	7.01	7.00	11.00	4.09	4.06	4.07	1B
7	Sodium carbonate	497-19-8	60	**1.46E-1**	15.01	4.01	11.01	15.02	4.08	8.00	7.00	11.00	4.07	3.08	1B
8	Sodium phosphate, tribasic; (Sodium hexametaphosphate; Calgon)	10124-56-8	500	**3.50E-3**	14.01	4.01	14.02	4.05	7.01	8.00	7.00	4.09	4.06	4.11	1B
9	Sodium hydroxide	1310-73-2	5	**3.50E-1**	14.01	11.01	14.02	11.00	4.07	10.00	4.11	4.12			1A
10	Sodium bicarbonate	144-55-8	300	**1.63E-3**	4.01	7.01	8.00	11.00	4.09	4.06	4.07	3.08	10.00	3.09	1B
11	Lithium hydroxide	1310-65-2	1	**3.50E-1**	14.01	4.01	11.01	14.02	4.05	7.01	8.00	7.00	11.00	4.08	1B
12	Potassium ferricyanide	13746-66-2	30	**1.17E-2**	15.01	11.01	15.02	4.07	3.02	3.09					1A
13	Manganese(II) chloride (1:2); (Manganous chloride)	7773-01-5	11.5	**3.04E-2**	4.05	7.00	7.01	8.00	4.08	4.06	4.09	4.10	11.00	4.07	1A
14	Molybdenum trioxide	1313-27-5	0.75	**4.67E-1**	11.01	6.00	15.01	11.00	15.02	4.10	4.06	2.00	10.00	3.02	1B

Figure A.5. Chemical and HCN Data for Test Case 5: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Tributyl phosphate	126-73-8	150	**2.33E-1**	15.00	7.00	11.00	5.00	3.00						1B
2	Phthalic acid	88-99-3	0.5	**3.50E+0**	15.00	11.00	12.00	3.02							1B
3	Potassium phosphate, monobasic	7778-77-0	50	**3.50E-1**	4.00	3.00	7.00								4
4	Nickel sulfate hexahydrate; (Nickel(II) sulfate hexahydrate)	10101-97-0	10	**8.75E-1**	2.00	4.00	5.00	7.01	10.00						4
5	Ammonium acetate	631-61-8	50	**7.00E-2**	4.00										2
6	Ethylenediaminetetraacetic acid, disodium salt	139-33-3	500	**7.00E-3**	4.00	5.00									4
7	Cupferron; (Ammonium-n-nitrosophenylhydroxylamine)	135-20-6	75	**1.17E-2**	15.01	2.00									1B
8	Sodium gluconate	527-07-1	15	**1.17E+0**	4.00										2
9	Ammonium formate	540-69-2	50	**1.05E-1**	4.00										2
10	Adipic acid	124-04-9	5	**1.75E-1**	14.01	7.00	3.07								1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Tributyl phosphate	126-73-8	300	**1.17E-1**	6.00	14.01	4.01	11.01	14.02	4.05	7.01	8.00	7.00	11.00	1B
2	Phthalic acid	88-99-3	0.5	**3.50E+0**	15.01	11.01	15.02	8.00	7.01	7.00	11.00	4.07	3.09	3.02	1B
3	Potassium phosphate, monobasic	7778-77-0	500	**3.50E-2**	15.01	11.01	7.01	8.00	4.07						1B
4	Nickel sulfate hexahydrate; (Nickel(II) sulfate hexahydrate)	10101-97-0	10	**8.75E-1**	8.00	4.07	3.08	3.09	10.00	3.02	3.10	2.00	3.01	5.10	4
5	Ammonium acetate	631-61-8	50	**7.00E-2**	15.01	11.01	4.05	7.00	11.00	4.09	4.10	4.07	3.05	16.02	1B
6	Ethylenediaminetetraacetic acid, disodium salt	139-33-3	500	**7.00E-3**	4.05	7.01	4.07	3.09	3.10	3.01	5.00	5.10			4
7	Cupferron; (Ammonium-n-nitrosophenylhydroxylamine)	135-20-6	75	**1.17E-2**	15.01	11.01	15.02	7.00	11.00	4.06	3.08	2.00	10.00	3.10	1B
8	Sodium gluconate	527-07-1	15	**1.17E+0**	15.01	11.01	15.02								1B
9	Ammonium formate	540-69-2	200	**2.63E-2**	15.01	15.02	11.01	4.07	4.02	4.09					1B
10	Adipic acid	124-04-9	5	**1.75E-1**	15.01	11.01	4.05	8.00	4.06	4.07	7.11	10.00	9.00	3.09	1B

Figure A.6. Chemical and HCN Data for Test Case 6: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Barium hydroxide	17194-00-2	3.12	5.61E-1	4.00	3.07	3.08	10.00	3.05						4
2	Zinc chloride	7646-85-7	40	4.38E-3	4.00	11.00	5.00	14.00	3.00						1A
3	Silica amorphous hydrated	7631-86-9	50	1.40E-2	19.00	10.00									4
4	Sodium hydride	7646-69-7	10	1.75E-1	18.00	11.00	14.02	14.01							1B
5	Sulfur dioxide	7446-09-5	1.96	8.11E-1	4.00	5.00	11.00	14.00							1A
6	Sodium hydroxide	1310-73-2	5	3.50E-1	4.00	14.01	14.02								1A
7	Hydrazine hydrate; (Hydrazine monohydrate)	7803-57-8	0.0625	5.60E+0	4.00	14.00	11.00								1A

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Barium hydroxide	17194-00-2	3.12	5.61E-1	14.01	14.02	4.01	4.07	8.00	7.00					1B
2	Zinc chloride	7646-85-7	50	3.50E-3	14.01	11.01	14.02	4.08	4.01	7.01	11.00	4.06	4.10	4.07	1A
3	Silica amorphous hydrated	7631-86-9	100	7.00E-3	15.01	11.00	3.07	3.09							1B
4	Sodium hydride	7646-69-7	7.5	2.33E-1	18.00	14.01	11.01	14.02	11.00	4.07					1B
5	Sulfur dioxide	7446-09-5	1.96	8.11E-1	14.01	11.01	14.02	4.08	4.05	7.01	7.00	11.00	4.02	4.09	1A
6	Sodium hydroxide	1310-73-2	5	3.50E-1	14.01	11.01	14.02	11.00	4.07	10.00	4.11	4.12			1A
7	Hydrazine hydrate; (Hydrazine monohydrate)	7803-57-8	0.0075	4.67E+1	7.00	7.01	6.00	14.01	11.01	14.02	11.00	4.05	4.06	4.07	1B

Figure A.7. Chemical and HCN Data for Test Case 7: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Potassium phosphate, monobasic	7778-77-0	50	**3.50E-2**	4.00	3.00	7.00								4
2	Ascorbic acid	50-81-7	500	**3.50E-3**	4.00	3.02	3.09	5.00							4
3	Perchloroethylene; (Tetrachloroethylene)	127-18-4	1560	**1.12E-3**	3.10	3.06	8.00	2.00							4
4	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**3.50E-3**	15.00	11.00	3.02	12.00							1B
5	Calcium(II) nitrate tetrahydrate (1:2:4)	13477-34-4	350	**5.00E-3**	16.00	4.00									1B
6	Sodium sulfate, anhydrous	7757-82-6	500	**7.00E-3**	4.00	5.00									4
7	Sodium carbonate	497-19-8	50	**3.50E-2**	4.00	5.00	15.01	16.02							1B
8	Sodium chloride	7647-14-5	300	**2.92E-2**	4.00	5.00	3.02	15.01	16.02						1B
9	Potassium chloride	7447-40-7	15	**1.17E-1**	4.00	3.02	3.08	16.01							1B
10	Sodium hydroxide	1310-73-2	5	**3.50E-1**	4.00	14.01	14.02								1A
11	Potassium permanganate	7722-64-7	14.4	**1.22E-1**	4.00	3.07	5.00	14.00							1A
12	Potassium hydroxide	1310-58-3	2	**8.75E-1**	4.00	14.01	14.02	11.00							1A
13	Ascorbic acid	50-81-7	500	**7.00E-4**	4.00	3.02	3.09	5.00							4
14	Magnesium chloride	7786-30-3	50	**3.50E-2**	4.00	3.11									2
15	Manganese(II) chloride (1:2); (Manganous chloride)	7773-01-5	11.5	**1.52E-1**	5.00	7.00	10.00								4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Potassium phosphate, monobasic	7778-77-0	500	**3.50E-3**	15.01	11.01	7.01	8.00	4.07						1B
2	Ascorbic acid	50-81-7	500	**3.50E-3**	15.01	4.01	11.01	4.08	8.00	7.00	11.00	4.09	4.06	4.10	1B
3	Perchloroethylene; (Tetrachloroethylene)	127-18-4	1560	**1.12E-3**	6.00	15.01	11.01	14.02	4.08	4.05	7.01	8.00	7.00	11.00	1A
4	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**3.50E-3**	14.02	4.08	4.05	8.00	7.00	11.00	4.09	4.06	4.10	3.09	1B
5	Calcium(II) nitrate tetrahydrate (1:2:4)	13477-34-4	350	**5.00E-3**	15.01	15.02	7.01	4.06	7.11	3.02					1B
6	Sodium sulfate, anhydrous	7757-82-6	500	**7.00E-3**	5.10	5.00	4.07	7.01							4
7	Sodium carbonate	497-19-8	60	**2.92E-2**	15.01	4.01	11.01	15.02	4.08	8.00	7.00	11.00	4.07	3.08	1B
8	Sodium chloride	7647-14-5	300	**2.92E-2**	15.01	4.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	4.09	1B
9	Potassium chloride	7447-40-7	15	**1.17E-1**	15.01	11.01	4.05	4.08	7.01	7.00	11.00	4.09	4.06	4.07	1B
10	Sodium hydroxide	1310-73-2	5	**3.50E-1**	14.01	11.01	14.02	11.00	4.07	10.00	4.11	4.12			1A
11	Potassium permanganate	7722-64-7	14.4	**1.22E-1**	14.01	4.01	11.01	14.02	4.08	4.05	7.01	8.00	11.00	4.09	1A
12	Potassium hydroxide	1310-58-3	2	**8.75E-1**	14.01	11.01	14.02	11.00	4.07	4.11	3.11	4.12			1A
13	Ascorbic acid	50-81-7	500	**7.00E-4**	15.01	4.01	11.01	4.08	8.00	7.00	11.00	4.09	4.06	4.10	1B
14	Magnesium chloride	7786-30-3	300	**5.83E-3**	11.01	4.08	4.05	7.01	8.00	7.00	11.00	4.01	4.06	7.10	1B
15	Manganese(II) chloride (1:2); (Manganous chloride)	7773-01-5	11.5	**1.52E-1**	4.05	7.00	7.01	8.00	4.08	4.06	4.09	4.10	11.00	4.07	1A

Figure A.8. Chemical and HCN Data for Test Case 8: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Strontium nitrate	10042-76-9	250	**7.00E-3**	4.00	7.01									4
2	Cesium chloride	7647-17-8	10	**3.50E-1**	4.00	5.00									4
3	Ferric ammonium sulfate; Sulfuric acid, ammonium iron(3e+) salt (2:1:1)	10138-04-2	25	**7.00E-2**	4.00	7.01	12.00	3.00	3.10						4
4	Ferric chloride	7705-08-0	25	**7.00E-2**	4.00	5.00	14.00								1B
5	Sodium bicarbonate	144-55-8	50	**3.50E-2**	4.00	5.00	3.09	11.00	16.00						1B
6	Gallium	7440-55-3	50	**7.00E-3**	4.00	15.00	3.11	3.03							1B
7	Silver nitrate	7761-88-8	15.7	**2.23E-2**	4.00	5.00	14.01	14.02	3.11						1B
8	Sodium chloride	7647-14-5	300	**5.83E-3**	4.00	5.00	3.02	15.01	16.02						1B
9	Potassium carbonate	584-08-7	150	**1.17E-2**	4.00										2
10	Sulfur	7704-34-9	2.5	**7.00E-1**	4.00	15.01									1B
11	Diphenyl; (Biphenyl)	92-52-4	6.5	**1.35E-1**	15.00										1B
12	Sodium acetate	127-09-3	300	**5.83E-3**	4.00	16.02	16.01								1B
13	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**3.50E-3**	15.00	11.00	3.02	12.00							1B
14	Ammonium, hexadecyltrimethyl-, bromide; (Hexadecyltrimethylammonium bromide)	57-09-0	0.75	**4.67E-1**	4.00										2
15	Aluminum oxide; (Alumina)	1344-28-1	15	**9.33E-2**	10.00	18.00	19.00								3

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Strontium nitrate	10042-76-9	60	**2.92E-2**	6.00	15.01	11.01	15.02	4.08	4.05	7.01	8.00	11.00	4.07	1B
2	Cesium chloride	7647-17-8	10	**3.50E-1**	4.08	4.05	7.01	7.00	11.00	4.09	4.07	3.08	7.11	10.00	4
3	Ferric ammonium sulfate; Sulfuric acid, ammonium iron(3e+) salt (2:1:1)	10138-04-2	25	**7.00E-2**	14.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	1B
4	Ferric chloride	7705-08-0	10	**1.75E-1**	6.00	15.01	11.01	15.02	4.08	4.05	11.00	4.09	4.10	4.07	1B
5	Sodium bicarbonate	144-55-8	300	**5.83E-3**	4.01	7.01	8.00	11.00	4.09	4.06	4.07	3.08	10.00	3.09	1B
6	Gallium	7440-55-3	50	**7.00E-3**	14.00	4.04	3.04	4.11	3.11						1B
7	Silver nitrate	7761-88-8	15.7	**2.23E-2**	13.00	14.01	4.01	11.01	14.02	4.05	7.01	8.00	7.00	11.00	1B
8	Sodium chloride	7647-14-5	300	**5.83E-3**	15.01	4.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	4.09	1B
9	Potassium carbonate	584-08-7	35	**5.00E-2**	15.01	15.02	11.01	4.01	11.00	4.07	3.08	3.09			1B
10	Sulfur	7704-34-9	30	**5.83E-2**	14.01	4.01	11.01	4.08	11.00	4.07	14.02	7.01	4.09	10.00	1B
11	Diphenyl; (Biphenyl)	92-52-4	60.5	**1.45E-2**	15.01	11.01	14.02	7.01	8.00	7.00	11.00	4.10	4.07	3.08	1B
12	Sodium acetate	127-09-3	300	**5.83E-3**	4.09	16.02	16.01	7.01							1B
13	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**3.50E-3**	14.02	4.08	4.05	8.00	7.00	11.00	4.09	4.06	4.10	3.09	1B
14	Ammonium, hexadecyltrimethyl-, bromide; (Hexadecyltrimethylammonium bromide)	57-09-0	0.75	**4.67E-1**	14.01	15.02	4.05	5.10	11.00	3.07	3.03				1B
15	Aluminum oxide; (Alumina)	1344-28-1	15	**9.33E-2**	10.00	3.03	19.00	3.05	4.07	11.01	15.01	15.02			1C

Figure A.9. Chemical and HCN Data for Test Case 9: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Dimethylacetamide, n,n-	127-19-5	1000	**9.83E-2**	4.01	11.00	7.01	7.00	3.09	3.10	3.07	5.00	3.11	16.01	1B
2	Pentane, n-	109-66-0	1500	**5.87E-2**	4.00	8.00	14.02	18.00							1B
3	Methyl alcohol; (Methanol)	67-56-1	2750	**1.24E-2**	4.00	4.01	5.00	15.00	8.00						1A
4	Copper(II) sulfate pentahydrate	7758-99-8	150	**2.10E-1**	14.01	14.02	3.10	3.09	3.02	3.08	3.07				1B
5	Toluene	108-88-3	4520	**5.68E-3**	15.00	8.00									2
6	Dimethyl sulfoxide; (DMSO)	67-68-5	750	**5.13E-2**	4.00	5.00	16.01	16.02	4.01						1B
7	Isopropyl alcohol	67-63-0	5000	**2.20E-2**	4.00	3.08	8.00	5.00	15.01						1A
8	Acetonitrile	75-05-8	537	**2.05E-1**	16.00	4.00									4
9	Methylene chloride	75-09-2	1940	**1.24E-1**	17.00	3.10	7.01	14.00	5.00						4
10	Chloroform	67-66-3	312	**4.16E-1**	2.00	3.10	3.09	8.00							4
11	Tetrahydrofuran	109-99-9	1470	**1.16E-1**	4.00	15.01	8.00	3.10	3.09						1A
12	Pyridine	110-86-1	600	**5.70E-2**	3.10	3.09	3.02	7.01	3.07						3
13	Ethyl ether	60-29-7	1500	**1.66E-2**	4.00	4.02	15.01	16.02	8.00						1A
14	Dimethylformamide, N,N-	68-12-2	269	**4.30E-1**	2.00	4.00	5.00	14.01	3.10						1B
15	Cyclohexane	110-82-7	1500	**3.73E-2**	4.00	15.01	16.02	3.11							1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Dimethylacetamide, n,n-	127-19-5	1000	**9.83E-2**	15.01	11.01	15.02	4.05	7.01	8.00	7.00	11.00	4.10	4.07	1B
2	Pentane, n-	109-66-0	1500	**5.87E-2**	15.01	8.00	14.02	18.00	11.01	4.05	7.01	7.00	11.00	3.05	1A
3	Methyl alcohol; (Methanol)	67-56-1	2750	**1.24E-2**	15.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	1A
4	Copper(II) sulfate pentahydrate	7758-99-8	150	**2.10E-1**	14.01	14.02	11.01	4.05	4.01	4.08	8.00	4.09	4.06	7.00	1B
5	Toluene	108-88-3	4520	**5.68E-3**	15.02	16.01	7.01	4.01	3.02	5.10	3.08	11.00	3.10	8.00	1A
6	Dimethyl sulfoxide; (DMSO)	67-68-5	4000	**9.63E-3**	4.01	4.08	4.05	7.01	8.00	7.00	11.00	4.09	4.06	4.10	1B
7	Isopropyl alcohol	67-63-0	1000	**1.10E-1**	6.00	15.01	4.01	11.01	4.08	4.05	7.01	8.00	7.00	4.09	1A
8	Acetonitrile	75-05-8	537	**2.05E-1**	17.00	14.01	11.01	14.02	4.08	7.01	11.00	4.09	4.06	4.10	1B
9	Methylene chloride	75-09-2	1940	**1.24E-1**	13.00	15.01	4.01	11.01	14.02	4.08	4.05	7.01	8.00	7.00	1A
10	Chloroform	67-66-3	312	**4.16E-1**	15.01	4.01	11.01	4.08	7.01	8.00	7.00	4.02	4.09	4.06	1A
11	Tetrahydrofuran	109-99-9	1470	**1.16E-1**	10.00	15.01	8.00	3.10	3.09	7.01	4.07	4.06	15.02	11.00	1A
12	Pyridine	110-86-1	15	**2.28E+0**	14.01	4.01	11.01	4.08	4.05	7.01	7.00	11.00	4.06	4.10	1B
13	Ethyl ether	60-29-7	1500	**1.66E-2**	15.01	11.01	4.08	4.05	7.01	8.00	7.00	11.00	4.02	4.10	1A
14	Dimethylformamide, N,N-	68-12-2	272	**4.25E-1**	13.00	14.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	1B
15	Cyclohexane	110-82-7	1000	**5.60E-2**	15.01	15.02	4.08	7.01	8.00	7.00	11.00	4.07	3.05	3.09	1B

Figure A.10. Chemical and HCN Data for Test Case 10: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Sodium phosphate, tribasic; (Sodium hexametaphosphate; Calgon)	10124-56-8	500	**3.50E-2**	14.01	3.11									1B
2	Sodium chloride	7647-14-5	300	**2.92E-2**	4.00	5.00	3.02	15.01	16.02						1B
3	Sodium nitrite	7632-00-0	1	**8.75E-1**	4.00	7.01	3.08	13.00	5.00						4
4	Potassium bromide	7758-02-3	250	**8.40E-2**	4.00	8.00	3.11								4
5	Sodium nitrate	7631-99-4	7.5	**1.40E+0**	4.00	5.00									4
6	Calcium chloride dihydrate	10035-04-8	500	**2.10E-2**	19.00										3
7	Potassium nitrate	7757-79-1	20	**8.75E-2**	4.00	5.00	12.00	3.09	13.00						4
8	Tetrasodium pyrophosphate	7722-88-5	25	**7.00E-2**	4.00										2

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Sodium phosphate, tribasic; (Sodium hexametaphosphate; Calgon)	10124-56-8	500	**3.50E-2**	14.01	4.01	14.02	4.05	7.01	8.00	7.00	4.09	4.06	4.11	1B
2	Sodium chloride	7647-14-5	300	**2.92E-2**	15.01	4.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	4.09	1B
3	Sodium nitrite	7632-00-0	1	**8.75E-1**	13.00	15.01	4.08	4.05	7.01	7.00	11.00	4.09	4.06	4.10	1B
4	Potassium bromide	7758-02-3	250	**8.40E-2**	11.01	15.02	8.00	4.05	4.02	4.01	7.01	7.00	4.07	3.05	1B
5	Sodium nitrate	7631-99-4	7.5	**1.40E+0**	13.00	15.01	11.01	4.05	7.01	4.07	10.00	3.10	3.07	5.00	1B
6	Calcium chloride dihydrate	10035-04-8	500	**2.10E-2**	14.01	4.01	3.03	5.00	5.10						1B
7	Potassium nitrate	7757-79-1	7.5	**2.33E-1**	13.00	15.01	11.01	15.02	4.08	4.05	7.01	11.00	4.09	4.10	1B
8	Tetrasodium pyrophosphate	7722-88-5	25	**7.00E-2**	15.01	15.02	11.01	4.01							1B

Figure A.11. Chemical and HCN Data for Test Case 11: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ethyl hexanoic acid, 2-; (Butyl ethyl acetic acid)	149-57-5	125	**2.80E-1**	4.00	5.00	14.01	16.02	3.10						1B
2	Calcium carbide	75-20-7	50	**3.81E+0**	18.00	3.11	3.12	3.06	14.00						1B
3	Chlorodifluoromethane; (Freon 22; CFC 22)	75-45-6	30000	**1.59E-2**	4.00	5.00	17.00	3.08							1C
4	Hexane	110-54-3	11600	**7.97E-3**	4.00	7.01	7.00	5.00	8.00						4
5	Methyl alcohol; (Methanol)	67-56-1	2750	**4.51E-2**	4.00	4.01	5.00	15.00	8.00						1A
6	Acetonitrile	75-05-8	537	**4.09E-1**	16.00	4.00									4
7	Isopropyl alcohol	67-63-0	5000	**2.20E-2**	4.00	3.08	8.00	5.00	15.01						1A
8	Ethylene glycol	107-21-1	100	**1.55E+0**	15.00	3.06	7.00	3.09	5.00						1B
9	Acetone	67-64-1	7600	**1.39E-1**	16.00	8.00									1B
10	Xylenes	1330-20-7	3990	**2.86E-2**	15.00	8.00	5.00								2
11	Ethyl acetate	141-78-6	1500	**8.40E-2**	4.00	4.02	11.00	4.01	12.00						4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ethyl hexanoic acid, 2-; (Butyl ethyl acetic acid)	149-57-5	500	**7.00E-2**	14.01	4.01	11.01	4.05	7.01	8.00	11.00	4.10	4.07	3.02	1B
2	Calcium carbide	75-20-7	50	**3.81E+0**	14.01	4.01	11.01	14.02	7.01	11.00	4.07	3.06	3.11	3.12	1B
3	Chlorodifluoromethane; (Freon 22; CFC 22)	75-45-6	30000	**1.59E-2**	17.00	15.01	11.01	4.08	7.01	8.00	7.00	11.00	4.09	4.06	1B
4	Hexane	110-54-3	11600	**7.97E-3**	17.00	14.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	1B
5	Methyl alcohol; (Methanol)	67-56-1	2750	**4.51E-2**	15.01	4.01	11.01	15.02	4.08	4.05	7.01	8.00	7.00	11.00	1A
6	Acetonitrile	75-05-8	537	**4.09E-1**	17.00	14.01	11.01	14.02	4.08	7.01	11.00	4.09	4.06	4.10	1B
7	Isopropyl alcohol	67-63-0	1000	**1.10E-1**	6.00	15.01	4.01	11.01	4.08	4.05	7.01	8.00	7.00	4.09	1A
8	Ethylene glycol	107-21-1	100	**1.55E+0**	15.01	4.01	11.01	4.08	4.05	7.01	8.00	7.00	11.00	4.09	1A
9	Acetone	67-64-1	7600	**1.39E-1**	15.01	11.01	15.02	4.08	4.05	7.01	8.00	4.06	4.07	3.05	1A
10	Xylenes	1330-20-7	3990	**2.86E-2**	14.01	11.01	15.02	4.05	7.01	8.00	7.00	11.00	4.02	4.09	1A
11	Ethyl acetate	141-78-6	1500	**8.40E-2**	15.01	4.01	11.01	15.02	4.05	7.01	8.00	11.00	4.02	4.09	1B

Figure A.12. Chemical and HCN Data for Test Case 12: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.00	11.00	2.00	5.00	4.00						1B
2	Methylphenol, 4-; (p-Cresol)	106-44-5	100	**3.50E-2**	14.00	11.00	13.00	7.01	3.00						1B
3	Mercury hydroxide	12135-13-6	0.117	**2.99E+1**	7.01	14.00	3.09	5.00	3.07	7.00					1A

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.01	11.01	14.02	4.08	7.01	8.00	11.00	4.07	2.00	2.02	1B
2	Methylphenol, 4-; (p-Cresol)	106-44-5	110	**3.18E-2**	14.01	11.01	14.02	7.01	4.05	8.00	4.01	7.00	4.08	11.00	1B
3	Mercury hydroxide	12135-13-6	0.117	**2.99E+1**	14.01	11.01	14.02	7.01	4.08	4.01	11.00	4.09	7.00	4.06	1A

Figure A.13. Chemical and HCN Data for Test Case 13: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.00	11.00	2.00	5.00	4.00						1B
2	Methylphenol, 4-; (p-Cresol)	106-44-5	100	**3.50E-2**	14.00	11.00	13.00	7.01	3.00						1B
3	Mercury hydroxide	12135-13-6	0.117	**2.99E+1**	7.01	14.00	3.09	5.00	3.07	7.00					1A
4	Sodium nickelate (Liquids)	z-0073	3	**1.17E+0**	13.00	2.00	7.00	10.00	9.00	3.07	3.06	3.11			4
5	Methyl thiocyanate	556-64-9	75	**4.67E-2**	11.00	3.11	3.09	3.10							4
6	Glyceryl monostearate; (Octadecanoic acid, monoester with 1,2,3-	31566-31-1	50	**7.00E-2**	4.00										2

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Trichloroacetic acid	76-03-9	15	**2.33E-1**	14.01	11.01	14.02	4.08	7.01	8.00	11.00	4.07	2.00	2.02	1B
2	Methylphenol, 4-; (p-Cresol)	106-44-5	110	**3.18E-2**	14.01	11.01	14.02	7.01	4.05	8.00	4.01	7.00	4.08	11.00	1B
3	Mercury hydroxide	12135-13-6	0.117	**2.99E+1**	14.01	11.01	14.02	7.01	4.08	4.01	11.00	4.09	7.00	4.06	1A
4	Sodium nickelate (Liquids)	z-0073	1.5	**2.33E+0**	13.00	7.01	4.07	3.08	2.00	10.00	9.00	3.09	3.02	3.10	4
5	Methyl thiocyanate	556-64-9	84.9	**4.12E-2**	11.00	15.01	15.02	8.00	7.01	4.05	4.07	10.00			1B
6	Glyceryl monostearate; (Octadecanoic acid, monoester with 1,2,3-	31566-31-1	15	**2.33E-1**	4.00	3.00									4

Figure A.14. Chemical and HCN Data for Test Case 14: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Butanenitrile; (Butyronitrile)	109-74-0	100	**3.50E-2**	5.00	14.01	7.00	11.00	3.02	3.08	16.02				1B
2	Phenylene diisocyanate, 1,4-	104-49-4	35	**1.00E-1**	4.00	14.02									1B
3	Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)	608-73-1	4	**8.75E-1**	2.00	4.00	12.00	5.00							4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Butanenitrile; (Butyronitrile)	109-74-0	100	**3.50E-2**	4.01	4.08	4.05	7.01	7.00	11.00	4.06	4.10	4.07	5.10	1B
2	Phenylene diisocyanate, 1,4-	104-49-4	35	**1.00E-1**	14.02	11.00	16.01	4.07							1B
3	Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)	608-73-1	4	**8.75E-1**	7.01	8.00	7.00	11.00	4.10	4.07	2.00	3.05	3.09	3.02	4

Figure A.15. Chemical and HCN Data for Test Case 15: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Butanenitrile; (Butyronitrile)	109-74-0	100	**3.50E-2**	5.00	14.01	7.00	11.00	3.02	3.08	16.02				1B
2	Phenylene diisocyanate, 1,4-	104-49-4	35	**1.00E-1**	4.00	14.02									1B
3	Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)	608-73-1	4	**8.75E-1**	2.00	4.00	12.00	5.00							4
4	Dichlorobenzene, p-	106-46-7	400	**8.75E-3**	3.00	7.00	5.00								3
5	Polychlorinated biphenyl (Aroclor 1016); (Chlorodiphenyl (41% Cl))	12674-11-2	1	**3.50E+0**	2.00	7.01	10.00	3.09	3.10	7.00	3.06	3.11			3

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Butanenitrile; (Butyronitrile)	109-74-0	100	**3.50E-2**	4.01	4.08	4.05	7.01	7.00	11.00	4.06	4.10	4.07	5.10	1B
2	Phenylene diisocyanate, 1,4-	104-49-4	35	**1.00E-1**	14.02	11.00	16.01	4.07							1B
3	Benzene hexachloride; (Hexachlorocyclohexane, mixed isomers)	608-73-1	4	**8.75E-1**	7.01	8.00	7.00	11.00	4.10	4.07	2.00	3.05	3.09	3.02	4
4	Dichlorobenzene, p-	106-46-7	60	**5.83E-2**	13.00	15.01	4.01	11.01	15.02	7.01	8.00	4.02	4.09	4.10	1B
5	Polychlorinated biphenyl (Aroclor 1016); (Chlorodiphenyl (41% Cl))	12674-11-2	300	**1.17E-2**	15.01	11.01	15.02	4.05	4.10	3.05	7.11	3.02	3.09	3.10	1B

Figure A.16. Chemical and HCN Data for Test Case 16: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Bromochlorobenzene, p-	106-39-8	50	**7.00E-2**	4.00	3.00									4
2	Ceric ammonium nitrate	16774-21-3	200	**1.75E-2**	4.00	3.11	7.01	3.02							4
3	Sodium nickel oxide (Liquid)	37367-09-2	2.33	**1.50E+0**	13.00	2.00	7.00	10.00	9.00	3.07	3.06	3.11			4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Bromochlorobenzene, p-	106-39-8	50	**7.00E-2**	4.00	3.00									4
2	Ceric ammonium nitrate	16774-21-3	50	**7.00E-2**	13.00	15.01	11.01	15.02	3.08	7.11	3.02				1B
3	Sodium nickel oxide (Liquid)	37367-09-2	1.16	**3.02E+0**	13.00	7.01	4.07	3.08	2.00	10.00	9.00	3.09	3.02	3.10	4

Figure A.17. Chemical and HCN Data for Test Case 17: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Bromochlorobenzene, p-	106-39-8	50	**7.00E-2**	4.00	3.00									4
2	Ceric ammonium nitrate	16774-21-3	200	**1.75E-2**	4.00	3.11	7.01	3.02							4
3	Sodium nickel oxide (Liquid)	37367-09-2	2.33	**1.50E+0**	13.00	2.00	7.00	10.00	9.00	3.07	3.06	3.11			4
4	Thorium oxide; (Thorium dioxide)	1314-20-1	500	**7.00E-3**	2.00	3.10	3.09	3.02							3
5	Diethylene glycol diacetate; (2,2'-oxybisethanol diacetate)	628-68-2	500	**7.00E-3**	15.01										1B
6	Barium sulfate	7727-43-7	350	**1.00E-2**	10.00										3

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Bromochlorobenzene, p-	106-39-8	50	**7.00E-2**	4.00	3.00									4
2	Ceric ammonium nitrate	16774-21-3	50	**7.00E-2**	13.00	15.01	11.01	15.02	3.08	7.11	3.02				1B
3	Sodium nickel oxide (Liquid)	37367-09-2	1.16	**3.02E+0**	13.00	7.01	4.07	3.08	2.00	10.00	9.00	3.09	3.02	3.10	4
4	Thorium oxide; (Thorium dioxide)	1314-20-1	500	**7.00E-3**	4.01	7.01	4.06	4.07	2.00	2.01	2.02	3.09	3.02	3.10	4
5	Diethylene glycol diacetate; (2,2'-oxybisethanol diacetate)	628-68-2	500	**7.00E-3**	15.01	11.01	15.02	7.01	7.00	11.00	5.00	5.10			1B
6	Barium sulfate	7727-43-7	50	**7.00E-2**	11.01	4.01	4.08	4.06	11.00	10.00					1B

Figure A.18. Chemical and HCN Data for Test Case 18: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Pentachloroethane	76-01-7	500	**7.00E-3**	3.00	16.00									3
2	Sodium cacodylate; (Sodium dimethylarsinate)	124-65-2	40	**8.75E-2**	4.00	5.00	10.00	16.00							1B
3	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**7.00E-3**	15.00	11.00	3.02	12.00							1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Pentachloroethane	76-01-7	500	**7.00E-3**	15.01	11.01	15.02	8.00	7.01	7.00	4.01	4.10	7.11	10.00	1B
2	Sodium cacodylate; (Sodium dimethylarsinate)	124-65-2	4	**8.75E-1**	15.01	15.02	4.08	4.05	4.07	5.00					1B
3	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**7.00E-3**	14.02	4.08	4.05	8.00	7.00	11.00	4.09	4.06	4.10	3.09	1B

Figure A.19. Chemical and HCN Data for Test Case 19: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Pentachloroethane	76-01-7	500	**7.00E-3**	3.00	16.00									3
2	Sodium cacodylate; (Sodium dimethylarsinate)	124-65-2	40	**8.75E-2**	4.00	5.00	10.00	16.00							1B
3	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**7.00E-3**	15.00	11.00	3.02	12.00							1B
4	Hexanol, n-; (n-Hexyl alcohol)	111-27-3	60	**5.83E-2**	14.01	16.02	4.00								1B
5	Trimethyloctane, 2,4,6-	62016-37-9	1500	**2.33E-3**	15.01	15.02	11.00								1B
6	Strychnine sulfate (2:1)	60-41-3	5	**7.00E-1**	7.00	7.01	11.00	3.07	5.00	4.01					4

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Category
1	Pentachloroethane	76-01-7	500	**7.00E-3**	15.01	11.01	15.02	8.00	7.01	7.00	4.01	4.10	7.11	10.00	1B
2	Sodium cacodylate; (Sodium dimethylarsinate)	124-65-2	4	**8.75E-1**	15.01	15.02	4.08	4.05	4.07	5.00					1B
3	Tris-hydroxymethylaminomethane; (THAM)	77-86-1	500	**7.00E-3**	14.02	4.08	4.05	8.00	7.00	11.00	4.09	4.06	4.10	3.09	1B
4	Hexanol, n-; (n-Hexyl alcohol)	111-27-3	60	**5.83E-2**	14.01	6.00	4.01	11.01	14.02	4.08	4.05	7.01	8.00	7.00	1B
5	Trimethyloctane, 2,4,6-	62016-37-9	1500	**2.33E-3**	11.01	16.02	16.01	3.05	11.00						1B
6	Strychnine sulfate (2:1)	60-41-3	5	**7.00E-1**	11.01	4.08	4.05	7.01	7.00	11.00	4.06				1B

Figure A.20. Chemical and HCN Data for Test Case 20: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Oxalic acid, anhydrous; (Ethanedioic acid)	144-62-7	500	**7.00E-3**	4.00	14.01	16.02	11.00	3.11						1A
2	Trimethylpyridine, 2,4,6-	108-75-8	150	**2.33E-2**	16.00	7.00	11.00								1B
3	Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)	78-42-2	12.5	**2.80E-1**	4.00	15.02	16.01								1B

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Oxalic acid, anhydrous; (Ethanedioic acid)	144-62-7	40	**8.75E-2**	14.01	4.01	11.01	14.02	4.08	7.01	7.00	11.00	4.09	4.06	1A
2	Trimethylpyridine, 2,4,6-	108-75-8	150	**2.33E-2**	15.01	11.01	15.02	4.05	7.01	7.00	4.07				1B
3	Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)	78-42-2	12.5	**2.80E-1**	15.01	15.02	7.11	10.00	3.09	3.02	3.10	3.01	3.11	3.07	1B

Figure A.21. Chemical and HCN Data for Test Case 21: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Oxalic acid, anhydrous; (Ethanedioic acid)	144-62-7	500	**7.00E-3**	4.00	14.01	16.02	11.00	3.11						1A
2	Trimethylpyridine, 2,4,6-	108-75-8	150	**2.33E-2**	16.00	7.00	11.00								1B
3	Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)	78-42-2	12.5	**2.80E-1**	4.00	15.02	16.01								1B
4	Chlorthiophos	21923-23-9	7.8	**4.49E-1**	6.00	7.00	7.01	11.00	3.08	3.07	4.01				4
5	Potassium chromate(VI)	7789-00-6	6	**5.83E-1**	2.00	4.00	5.00	3.10	14.00						1A

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Oxalic acid, anhydrous; (Ethanedioic acid)	144-62-7	40	**8.75E-2**	14.01	4.01	11.01	14.02	4.08	7.01	7.00	11.00	4.09	4.06	1A
2	Trimethylpyridine, 2,4,6-	108-75-8	150	**2.33E-2**	15.01	11.01	15.02	4.05	7.01	7.00	4.07				1B
3	Tri(2-ethylhexyl) phosphate; (Tris(2-ethylhexyl)phosphate)	78-42-2	12.5	**2.80E-1**	15.01	15.02	7.11	10.00	3.09	3.02	3.10	3.01	3.11	3.07	1B
4	Chlorthiophos	21923-23-9	7.8	**4.49E-1**	6.00	15.01	4.01	11.01	4.08	4.05	7.01	7.00	11.00	4.07	1B
5	Potassium chromate(VI)	7789-00-6	12.5	**2.80E-1**	14.01	4.01	11.01	4.08	4.05	7.01	11.00	4.09	4.07	2.00	1A

Figure A.22. Chemical and HCN Data for Test Case 22: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ferric nitrate	10421-48-4	21.7	**1.61E-1**	15.00										1B
2	Bismuth	7440-69-9	40	**8.75E-2**	7.00	11.00									3
3	Trimethoxysilane	2487-90-3	10	**3.50E-1**	4.00										2

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ferric nitrate	10421-48-4	250	**1.40E-2**	15.02	15.01	11.01	4.07	4.08	4.08	11.00				1B
2	Bismuth	7440-69-9	40	**8.75E-2**	4.05	4.09	7.00	7.01	3.02	3.04	4.08	7.11			4
3	Trimethoxysilane	2487-90-3	4.15	**8.43E-1**	16.02	15.01	11.00								1B

Figure A.23. Chemical and HCN Data for Test Case 23: 2007 and 2011 Versions of the CMM.

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ferric nitrate	10421-48-4	21.7	**1.61E-1**	15.00										1B
2	Bismuth	7440-69-9	40	**8.75E-2**	7.00	11.00									3
3	Trimethoxysilane	2487-90-3	10	**3.50E-1**	4.00										2
4	Zirconium silane	z-0089	16.2	**2.16E-1**	4.00	3.00									4
5	Silicon(II) oxide; (Silicon oxide)	10097-28-6	50	**7.00E-2**	18.00										2

No.	Chemical Compound	CASRN	Conc. Limit PAC-n (mg/m^3)	Hazard Index (HI)	Health code Numbers (HCNs)										
					HCN-1	HCN-2	HCN-3	HCN-4	HCN-5	HCN-6	HCN-7	HCN-8	HCN-9	HCN-10	Cate-gory
1	Ferric nitrate	10421-48-4	250	**1.40E-2**	15.02	15.01	11.01	4.07	4.08	4.08	11.00				1B
2	Bismuth	7440-69-9	40	**8.75E-2**	4.05	4.09	7.00	7.01	3.02	3.04	4.08	7.11			4
3	Trimethoxysilane	2487-90-3	4.15	**8.43E-1**	16.02	15.01	11.00								1B
4	Zirconium silane	z-0089	16.2	**2.16E-1**	15.01	11.01	15.02	4.08	7.01	4.09	4.06	4.10	4.07	10.00	1A
5	Silicon(II) oxide; (Silicon oxide)	10097-28-6	50	**7.00E-2**	18.00	15.01	11.01	15.02	7.01	4.07					1B

Figure A.24. Chemical and HCN Data for Test Case 24: 2007 and 2011 Versions of the CMM.

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