User's Guide and description of "Default Methodology for Analysis of Airborne Exposure to Mixtures of Chemicals in Emergencies"

Introduction:

What follows is a summary of the Excel Workbook set up to automatically apply the SCAPA Mixture Methodology (published in Annals of Occupational and Environmental Hygiene, Volume 14(9), 609-617, 1999) to a user-supplied mixture of chemicals. The workbook comprises six worksheets, one of which is a lookup tabulation of Health Code Numbers (HCNs) and Temporary Emergency Exposure Limits (TEELs) This is updated periodically, and currently has HCNs for 2234 chemicals (TEELs Rev 19) and TEELs for 2519 chemicals (TEELs Rev 20). HCNs are being developed for the added chemicals in "TEELs Rev 20". HCNs and TEELs are accessed via the Chemical Abstract Services Registry Number (CASRN) or substitute (e.g., "z" numbers), by the program used to calculate Hazard Indices (HIs).

Only the "Input" worksheet is accessible to the user. The other worksheets are password "protected" to retain the integrity of the software. The "Input" worksheet has room for entry of up to thirty (30) chemicals. Few mixtures are likely to involve more chemicals If the user has a need to analyze a mixture of more than thirty chemicals, it will be necessary to contact the authors (at craigdk@earthlink.net, or craigdk@comcast.net,or rocky.petrocchi@wgint.com). All the results of interest are displayed on the "Output" worksheet. All worksheets are automatically completed when the Excel workbook is calculated (i.e., press the "Ctrl" and "=" together, or press "F9". On the Macintosh, press the "Apple" or "Command" and "=" keys together).

Although all worksheets other than "Input" and "HCN-TEEL" are protected, the User can nonetheless change the way each sheet is printed (go to "File", then "Page setup" and make the desired changes).

As a practical note, the Excel workbook has macros that do all of the lookups and calculations. Excel has three levels of security (high, medium, low) on macro-containing Excel files since macros can contain computer viruses. If your Excel security level is "High," your computer may not execute all of the macros or may not execute any of them. Excel security should be set to no more than "Medium" for the macros to execute. To check Excel security level, open an Excel file, and go to Tools→ Macro→ Security→ Security Level. Once the security level in any Excel file is set, it will stay that way for all Excel files until changed again. If an Excel window about enabling/disabling macros appears, click the "Enable Macros" button to execute the macros.

Mixture Methodology

1 Delete the current contents for ten chemicals on the Input worksheet (Table 1). They are there for illustrative purposes only.

2 List all chemicals in the mixture ("Input" column B).

3 List the Chemical Abstract Service Registry Number [CASRN] of all these chemicals ("Input" column C). If CASRN is not known, highlight column B of the "HCN-TEEL" worksheet, press Control-F or go to "Find" under the Edit menu, type in the chemical name and Enter. If the chemical is in the list, it will be highlighted. **Use the exact entry in column C for the CASRN,** since this is the primary parameter that the Workbook uses for its HCN and TEEL lookups. Chemicals for which CASRNs have not been found are listed in the lookup table with "z" substitute numbers. A few of these chemical substance names are prefixed with "zz" to place them at the bottom of the table when sorted by name.

4 Enter the receptor point of interest (e.g., offsite, onsite at 600 m, 300 m, 200 m, or 100 m, local at 30 m) ("Input" column D). This parameter is not used in the workbook computations, but guides the user in choosing the concentration limit.

5 Determine the concentration limit ($\mathbf{L_i}$)at that receptor point (e.g., TEEL-2) for the specific application (e.g., emergency planning, hazard assessment, etc.) ("Input" column E). *If a chemical has ERPGs, the ERPGs are the relevant TEELs.*

6 Calculate or otherwise obtain the airborne concentration ($\mathbf{C_i}$) of each chemical "i" at the receptor point ("Input" column F).

From this point forward, the rows and columns in all subsequent worksheets are automatically completed when the workbook is calculated.

7 The workbook calculates the Hazard Index (HI_i) for each chemical
i.e., $\mathbf{HI_i = C_i / L_i}$
for each receptor point ("Import" column E).
Individual hazard indices must all be ≤ 1.00.

8 Initially, the workbook sums all the HI_I values to determine acceptability of the scenario being evaluated, and whether protective actions or administrative controls should to be applied,

i.e., $$\sum_{i=1}^{n} HI_i = HI_1 + HI_2 + \ldots + HI_n.$$

("Import" column E, last row).

9 If this meets the criterion

$$\sum_{i=1}^{n} HI_i \leq 1$$

there is no need to proceed. This sum is **bolded red if > 1.00**.

If $\sum HI_i > 1.00$, then using the Health Code Number (HCN) table (both HCNs and TEELs are included in the "lookup" worksheet "HCN-TEEL"), the workbook**:**

10 Determines the toxicologic classification of each chemical (i.e., their HCNs) ("Import" columns E, F, G, H, I, J, K, L, M, N) from the "lookup" worksheet**;**

11 Determines the category of each chemical ("Import" column O)**;**
The category gives the concentration-limit classification used to determine whether the toxicologic consequences of exposure to a chemical are concentration-dependent, dose-dependent, or both. While the category is used in HCN and TEEL determination, it is not used explicitly in the mixture methodology. However, it may aid the user in determining whether a longer or shorter time period than the recommended 15-minute duration may logically be used in measuring or modeling the user supplied concentration at the receptor point of interest ("Input" column F)**;**

12 Sums the HIs of all chemicals having the same HCNs. The sums must all be less than or equal to 1.00 for the exposure to be within established limits. For the user's convenience, all sums of **HI s ≥ 0.5** are **bolded red;**

This is done automatically in the subsequent worksheets in this workbook; for example, the HIs for those chemicals that are carcinogens (HCNs 1 and 2), chronic, systemic toxins HCN = 3.00, 3.01-3.12), acute systemic toxins (HCN = 4.00, 4.01, 4.02), reproductive toxins (HCN = 5.00), etc. Irritants are a special case, in so far as they may be severe (HCN = 14.00, 14.01, 14.02), moderate (HCN = 15.00, 15.01, 15.02), or mild (HCN = 16.00, 16.01, 16.02). These are added together, but weighted by severity (i.e., multiplied by 1.00 for severe, 0.5 for moderate, 0.25 for mild). HCNs 14.00, 15.00, and 16.00 are used for irritants that affect eyes, skin and mucous membranes, and appropriately weighted HIs of chemicals having these HCNs must be added to HIs for chemicals affecting only the eyes (HCN = 14.01, 15.01, 16.01) or only the skin and nose (HCN = 14.02, 15.02, 16.02). This Excel workbook will carry out these computations automatically for all chemicals on the HCNs and TEELs lookup table. Chemicals having no HCNs in this "lookup" table are those added to the TEEL list for "TEELs Rev 20".

The individual worksheets, together with the headings for each column in that worksheet, follow**:**

Worksheet 1 – Required user Input:

Table 1: Chemical Compounds, Receptor Point, Concentration Limit and Concentrations of Chemicals in Mixture (print page 1, no more than 30 chemicals)

1 No. (Column A)

2 Chemical Compound (Column B)

3 CASRN (Column C)

4 Receptor Point (Column D)

5 Concentration Limit at Receptor Point, e.g., TEEL-n (Column E), where "n" is the appropriate TEEL level, i.e., -0, -1, -2, -3. TEEL-n is used to simplify the import routines, since if a chemical has ERPGs, the ERPGs are the relevant TEELs. Do NOT enter ERPG-1, -2, -3, as this will not work.

6 Concentration at Receptor Point (mg/m^3) (Column F). This is a user-determined and user-supplied parameter.

For release durations of fifteen minutes or more, concentrations for comparison with the appropriate guidelines should be calculated as the peak 15-minute time-weighted average (TWA) at the receptor points of interest[(4)]. For release durations of less than 15 minutes, concentrations for comparison with guideline values may be calculated over a shorter time period but, as a practical lower time limit, not less than one minute. For dose-dependent chemicals (chemical category 3) only, the concentration at the receptor point of interest may be calculated as the peak 60-minute TWA concentration if the peak 15-minute TWA value is too restrictive (e.g., HI > 1.0).

Note: The “Input” worksheet is <u>not</u> protected.

Worksheet 2 – Import (performed automatically):

Table 2: Hazard Index Calculation and HCNs for Chemicals in Mixture (print p 2)

1 No. (Column A)

2 Chemical Compound (Column B)

3 CASRN (Column C)

4 Concentration Limit $\mathbf{L_i}$ (mg/m3) (Column D)

TEEL-n is the "Input" column E lookup value from "HCN-TEEL" worksheet

5 Hazard Index (HI) (Column E), "Input" column F divided by "Import" column D.

USER: Check to see that all HI values in column E are less than or equal to 1.00. Individual chemical HIs > 0.5 are bolded red, indicating possible need for mitigative action. Check the sum of these HIs at the foot of the column. If this hazard Index sum is ≤ 1.00, then the exposure is within established limits and there is no need to consult the next worksheet.

6-16 Health Code Numbers (HCNs)

6 HCN-1 (Column F), Column E from "HCN-TEEL" worksheet

7 HCN-2 (Column G), Column F from "HCN-TEEL" worksheet

8 HCN-3 (Column H), Column G from "HCN-TEEL" worksheet

9 HCN-4 (Column I), Column H from "HCN-TEEL" worksheet

10 HCN-5 (Column J), Column I from "HCN-TEEL" worksheet

11 HCN-6 (Column K), Column J from "HCN-TEEL" worksheet

12 HCN-7 (Column L), Column K from "HCN-TEEL" worksheet

13 HCN-8 (Column M), Column L from "HCN-TEEL" worksheet

14 HCN-9 (Column N), Column M from "HCN-TEEL" worksheet

15 HCN-10 (Column O), Column N from "HCN-TEEL" worksheet

16 Category (Column P), Column O from "HCN-TEELs" worksheet

Row 34 Sum of Hazard Indices for all chemicals in Mixture (Column E, value **bolded red if > 1.00**)

Note: This worksheet, Import or Table 2, is protected.

Worksheet 3 - HIs by Mode (performed automatically):

Table 3: Summation of Hazard Indices by Mode of Toxic Action for Chemicals in Mixture (print pages 3 – 4)

1 No. (Column A).

2 Chemical Compound (Column B).

3 CASRN (Column C).

4-11 Hazard Indices for Chemicals with same HCNs (p 3)**:**

4 HCN = 1 or 2 Carcinogens (Column D), HIs with sum at foot of column.

5 HCN = 14, 15, or 16 Irritants (Column E), Weighted His with sum at foot of column.

6 HCN = 3 Chronic Systemic Toxins Column F), HIs with sum at foot of column.

7 HCN = 4 Acute Systemic Toxins (Column G), HIs with sum at foot of column.

8 HCN = 5 Reproductive Toxins (Column H), HIs with sum at foot of column.

9 HCN = 6 Cholinesterase Toxin (Column I), HIs with sum at foot of column.

10 HCN = 7 Nervous System Toxin (Column J), HIs with sum at foot of column.

11 HCN = 8 Narcotics (Column K), HIs with sum at foot of column.

12-18 Hazard Indices for Chemicals with same HCNs (p 4)**:**

12 HCN = 9 Respiratory Sensitizer (Column L), HIs with sum at foot of column.

13 HCN = 10 Chronic Respiratory Toxin (Column M), HIs with sum at foot of column.

14 HCN = 11 Acute Respiratory Toxin (Column N), HIs with sum at foot of column.

15 HCN = 12 Blood Toxin Anemia (Column O), HIs with sum at foot of column.

16 HCN = 13 Blood Toxin Methemoglobinemia (Column P), HIs with sum at foot of column.

17 HCN = 17 Asphyxiants (Column Q), HIs with sum at foot of column.

18 HCN = 18 Explosive, Flammable, Safety (Column R), HIs with sum at foot of column.

19 HCN = 19 and 20 Other & nuisance (Column S), HIs with sum at foot of column.

All "Sums of Toxic Mode or Endpoint-specific HIs" (Row 34 Columns D through S) must be ≤ 1.00. If not, individual HIs need to be examined to pinpoint which chemicals in the mixture are contributing most to the sum(s).

Note: Table 3 is protected.

Worksheet 4 – HIs by Target Organ (performed automatically)**:**

Table 4: Summation of Hazard Indices by Target Organ for Chemicals in Mixture (print pages 5 – 7).

1 No. (Column A).

2 Chemical Compound (Column B).

3 CASRN (Column C).

4-9 Hazard Indices for Chemicals with same HCNs (print page 5)**:**

4 HCN = 1, or 2 Carcinogens (Column D), HI sum at foot of column.

5 HCN = 1, 1.01, 2 or 2.01 Bladder Cancer (Column E), HI sum at foot of column.

6 HCN = 1, 1.02, 2 or 2.02 Liver Cancer (Column F), HI sum at foot of column.

7 HCN = 3.01 or 3 Bladder Toxin (Column G), HI sum at foot of column.

8 HCN = 3.02 or 3 Unspecified Hematological Effects (Column H), HI sum at foot of column.

9 HCN = 3.03 or 3 Bone Toxin (Column I), HI sum at foot of column.

10-15 Hazard Indices for Chemicals with same HCNs (print page 6)**:**

10 HCN = 3.04 or 3 Bone Marrow Toxin (Column J), HI sum at foot of column.

11 HCN = 3.05 or 3 Brain Toxin (Column K), HI sum at foot of column.

12 HCN = 3.06 or 3 Eye (Chronic ocular) (Column L), HI sum at foot of column.

13 HCN = 3.07 or 3 Gastrointestinal Tract Toxin (Column M), HI sum at foot column.

14 HCN = 3.08 or 3 Heart Toxin (Column N), HI sum at foot of column.

15 HCN = 3.09 or 3 Kidney Toxin (Column O), HI sum at foot of column.

16-21 Hazard Indices for Chemicals with same HCNs (print page 7)**:**

16 HCN = 3.10 or 3 Liver Toxin (Column P), HI sum at foot of column.

17 HCN = 3.11 or 3 Skin Toxin (Column Q), HI sum at foot of column.

18 HCN = 3.12 or 3 Skin Perforation (Column R), HI sum at foot of column.

19 HCN = 4.01 or 4 Eye (Acute, other than Irritation (Column S), HI sum at foot of column.

20 HCN = 4.02 or 4 Nose (Column T), HI sum at foot of column

21 HCN = 7.01 or 7 Central Nervous System (Column U), HI sum at foot of column.

All "Sums of Organ-specific HIs" (Row 34 Columns D through U) must be ≤ 1.00.

Note: Table 4 is protected.

Worksheet 5 – Output (performed automatically)**:**

Table 5: Mixture Methodology Output Summary (p 8).

1 Column A: No.

2 Column B: Chemicals in Mixture.

3 Column C: Chemical CASRN.

4 Column D: Individual Hazard Index (HI).

5 Column E: Sum of all His.

6 Column F: Blank.

7-8 Toxic Mode or Endpoint-specific HI s**:**

7 Column G: Mode or Endpoint.

8 Column H: HI sum ≥ 0.25.

9-10 Sum of Organ-specific HI s**:**

9 Column I: Organ.

10 Column J: HI sum ≥ 0.25.

HIs > 0.5 are bolded red

Note: This table summarizes information on Tables 2, 3, and 4. If the sum of all HIs ≤ 1 (Column E), there is no need to consult the right hand section. If all Endpoint-specific or Organ-specific HIs ≤ 1, exposure to the mixture is within established limits. Table 5 is protected.

Worksheet 6 – HCN-TEEL (used by the Workbook as a look-up table only)**:**
HCNs and TEELs in mg/m^3 (This look-up table will be updated periodically as TEELs and HCNs are derived for new chemicals or TEELs are otherwise changed)

1 Column A: No.
2 Column B Chemical Compound.
3 Column C: CASRN.
4 Column D: SAX number.
5 Column E-O: Health Code Numbers (HCNs 1-5) and Category.
6 Column P-S: TEELs (mg/m^3). If a chemical has ERPGs, the chemical name, CASRN and numbers are in **Bold**
7 Column T: Original units (ppm or mg/m^3). If the original units were ppm, then these values were converted to mg/m^3 so that all values are in the same units.

This worksheet is not protected and is not intended to be printed as part of the Chemical Mixture Methodology file. If a chemical is not listed, it may be added to the bottom of the lookup table (i.e., in row 2523 at the moment), along with its CASRN or substitute, default HCNs of 3.00 and 4.00 (in columns E and F), and appropriate user-supplied concentration limits (in columns P, Q, R and S).