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Air, Radiation and Toxics Division
Philadelphia, PA 19107

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Region III
Technical Guidance Manual
Risk Assessment

Chemical Indexing System for the Toxic Chemical Release Inventory Part I: Chronic Index

EPA Contact: Dr. Debra L. Forman

EPA
Region III

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The TRI database contains information about chemical releases and transfers from industrial manufacturers and processors (primary Standard Industrial Classification (SIC) codes 20-39) to environmental media. Since 1987, facilities meeting established thresholds have been required to report release data according to section 313 of the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA)[1]. To date, however, Agency tracking and analysis of the data has generally been limited to an evaluation of the relative amounts of chemicals released without regard for differences in chemical toxicity[2]. This guidance document presents a method for evaluating EPCRA chemical releases in terms of their toxicity and is intended to support enforcement targeting and strategic planning efforts with a more realistic evaluation of these chemical releases. The intent of this process is to place emphasis on the most toxic chemical releases reported under EPCRA §313. Furthermore, the technique provides a standard tool which reflects the dynamic operating system of EPCRA program development and scientific growth. The method also fulfils the EPA Region III mandate to utilize best science in its decision-making processes. The guidance is intended to be used as a screening tool to improve the quality and consistency of enforcement targeting and strategic planning for the EPCRA program in Region III. (EPA/903/R-93/002)

1. BACKGROUND

To date, analysis of the Toxic Chemical Release Inventory Database (TRI) has generally been limited to comparisons of the relative amounts of chemical releases without regard for differences in chemical toxicity[2]. While some methods have attempted to define relative toxicity in terms of ordinal or categorical scoring systems, the large uncertainties inherent in the analysis have limited the usefulness of the results[3,4]. This guidance serves as a refinement of previous methodologies[2,4,5] and offers a scheme for media-specific, multi-component Chemical Indexing which utilizes a dose-based approach to rank TRI chemical releases. In this paper, the first component of the Index is presented. It is termed a Multiple Component "Chronic Index" since it is based on both cancer and chronic noncancer effects of EPCRA chemicals. The results of the Chronic Index are intended to be used as a supplemental screening tool to refine planning and enforcement targeting efforts and focus resources on the most compelling problems. While the results of Phase I are intended as a priority screening tool for hazard identification, Phase II of the project focuses on evaluating the relative risks of targeted releases.

The Chronic Index is based on a combination of TRI emissions data and an estimate of relative dose,

rather than an ordinal or categorical scoring system. In this way, the resultant ranking retains more sensitivity to experimental data by preserving the relative intervals between adjacent calculated index values[6]. Moreover, because the results of the index are intended for hazard identification, the values are necessarily independent of calculated exposure and subsequent risk values[7].

Subsequent development of the Chemical Indexing System will include consideration of the acute toxicologic effects and potential chemical fate of TRI chemicals (see Figure 1). The Chemical Index is intended to enable identification of specific facilities estimated to contribute the greatest amount of toxic releases to the environment and as the project progresses, a database of index values assigned to each EPCRA facility will be collected for use with GIS mapping.

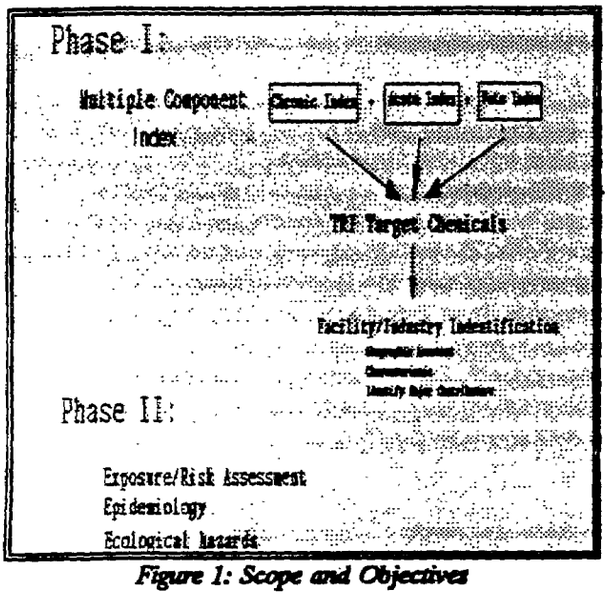

Figure 1: Scope and Objectives

Upon completion of Phase I of this project, Phase II will apply risk assessment methodologies to evaluate the specific human health exposure scenarios, and fate and transport modelling to assess exposure point concentrations of targeted chemicals. The epidemiologic literature will also be consulted to support evaluations concerning possible cause and effect relationships. This aspect provides additional support to decision-makers in the evaluation of perceived versus actual adverse health impacts of TRI emissions. Ecological considerations are also included in the overall assessment of the predicted impact of the TRI release.

2. METHODS

2.1. Primary Datasets: The TRI database (TRIS) is maintained by the U.S. EPA in Research Triangle Park, NC and is also a component file of the National Library of Medicine's TOXNET system. Agency access to the database and downloading procedures are available. Public access to TRI can be obtained by writing to:

U.S. EPA
P.O. Box 70266
Washington, D.C. 20024-0266
Attention: TRI Public Inquiry

In order to estimate the relative toxicity of TRI chemicals, a consistent criterion for comparison is required. The IRIS database of oral Reference Doses (RfD) and Cancer Slope Factors (CPF) was selected as the baseline for toxicity comparison for several reasons. Firstly, the database provides quantitative estimates of toxicity which are derived using a consistent, established procedure. This serves to standardize errors inherent in the database. Secondly, the RfD and CPF approval processes are endorsed by the EPA and are nationally recognized as a source of relative toxicity data. This serves to support future actions which might be based on the results of the Indexing procedure. For access to the IRIS database, contact the Risk Information Hotline at (513) 569-7254.

The IRIS database provides oral toxicity factors for most EPCRA chemicals. However, because IRIS supports all EPA programs with limited resources, IRIS toxicity data are not always available for all EPCRA chemicals.

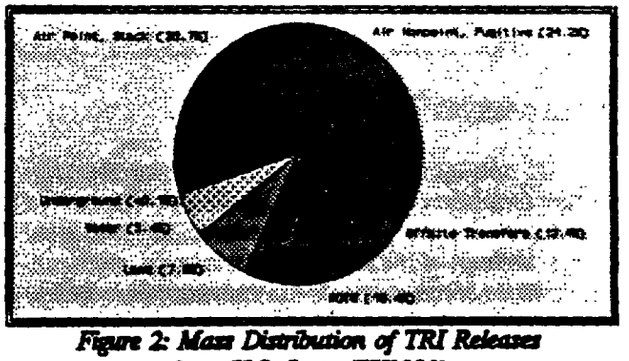

Figure 2: Mass Distribution of TRI Releases for a U.S. State (RY1990)

Figure 2 shows a sample dataset reported in one U.S. State for the 1990 reporting year (RY1990) where more than 50% of the pounds reported were released to the air medium. Of this amount, up to 87% of the fugitive

emissions can be accounted for using the toxicity information in IRIS. About 50% of the point source emissions can be expressed in terms of IRIS toxicity data (see Figure 3).

It is important to point out that depending on the industrial processes used and the availability of toxicity information, the percentage of chemical releases expressed in terms of the Chronic Index may vary from year to year. Nevertheless, each calculated facility index may be tracked to evaluate trends. Estimates of acute toxicity and chemical fate will be incorporated into the Index in forthcoming updates of this guidance which will serve to improve the percentage of TRI releases measured by the Index. Moreover, it is understood that the EPA-RfD (Reference Dose) and EPA-CRAVE (Carcinogen Risk and Verification Endeavor) workgroups approve new chemicals monthly and care should be taken to include the new chemicals as they become available.

In the absence of primary toxicity data (IRIS), the reported chemical releases are termed "residual releases" and are ranked according to the mass released (lb/yr). This list is then examined for candidate chemicals which may possess toxicity information from secondary sources.

2.2. Secondary Datasets: Secondary sources of toxicity data are investigated for possible inclusion of residual chemicals not represented by IRIS toxicity data. Generally, a provisional toxicity factor from a secondary source is investigated if a compound is identified in the top 90 percentile of the residual releases.

Some examples of secondary sources include the Health Effects Assessment Summary Tables (HEAST), provisional factors derived from intra- or inter-Agency sources, such as the Environmental Criteria Assessment Office, Office of Pollution Prevention and Toxic Substances and the National Toxicology Program, or the general literature. While this is not an exhaustive listing of secondary sources, the preferred hierarchy of toxicity sources is commensurate with the most to least rigorous level of Agency review.

In the absence of primary or secondary toxicity data, the residual releases are ranked according to pounds released per year and the ranking is included as a corollary to the Chronic Index report.

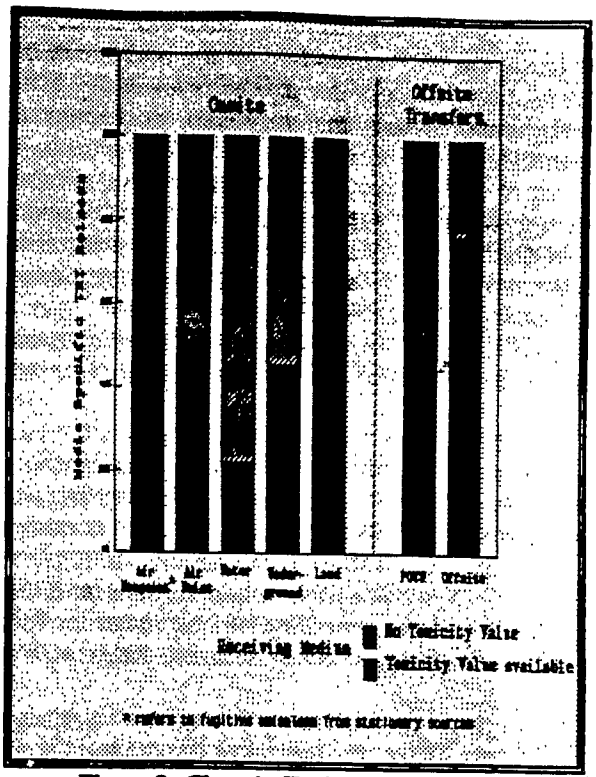

Figure 3: Chronic Toxicity Distribution (U.S. State) RY1990

2.3. Emphasis of Carcinogens vs. Non-Carcinogens: The Index System includes an adjustment to account for the policy relationship between carcinogenic versus noncarcinogenic regulations. This adjustment is not intended to imply biological significance of the individual toxic effects, but is included to remain consistent with Agency policies regarding regulation of risk and hazard levels for carcinogens and non-carcinogens. The adjustment is based solely on Agency policy which outlines the conditions for acceptable hazard and risk levels.

For noncarcinogens regulated under the Superfund Program, the National Contingency Plan (NCP) recommends concentrations "to which the human population, including sensitive subgroups, may be exposed without adverse effect during a lifetime or part of a lifetime, incorporating an adequate margin of safety."[8] Thus, the acceptable exposure level occurs at levels where there is no lasting deleterious effect. This has generally been interpreted as those concentrations equivalent to a hazard index of 1[12,13].

For carcinogens regulated under the Superfund Program, the NCP states that for the purpose of hazard identification, 'acceptable exposure levels are generally concentration levels that represent an excess upper bound lifetime cancer risk to an individual of between 10^{-4} and 10^{-6} using information on the relationship between dose and response.'[9] In addition to Superfund, other Agency programs also recommend this risk range for hazard identification of carcinogens. For example, rulemaking pursuant to The Clean Air Act Ammendments of 1990 discuss screening carcinogens for the early reduction plan at a risk level of 1×10^{-4} [10].

Thus, in accordance with policy statements regarding hazard identification, the hazard index level of 1 and the risk level of 1×10^{-4} represent acceptable limits for this purpose. The Chronic Index is computed in accordance with these policy statements by expressing the dose for noncarcinogens at a hazard index = 1 and the dose for carcinogens at 1×10^{-4} risk (approximately equivalent to a hazard index = 0.04)[11].

Additional refinements of the System will include grouping of the noncarcinogenic toxicity data in terms of target organ toxicity and if deemed appropriate, the development of an appropriate weighting system.

3. ALGORITHMS

3.1. Derivation of the Chronic Index: LOTUS spreadsheets were developed for data handling and analysis. The TRI release data was combined with the corresponding IRIS-approved oral RfD and/or CPF value to obtain an estimate of the relative toxicity of the TRI release. The resultant estimate is termed the Chronic Index.

The algorithm is based on the assumption that adverse health effects resulting from exposure to either carcinogens or noncarcinogens is due to some dosage received by the organism. Since the present form of IRIS toxicity data does not lend itself to direct comparison of carcinogenic and noncarcinogenic doses, a method was derived which normalizes the two dose scales. The resultant standardization permits comparison and equivalency ranking of both carcinogenic and noncarcinogenic TRI releases.

Reference points for determining relative hazard are identified according to Agency policies cited above[8,9,10]. The reference point for noncarcinogenic dose is calculated at a hazard index of 1 and the reference point for carcinogenic dose is equivalent to 1×10^{-4} risk.

Following dose calculation for carcinogens, the calculated doses are adjusted according to the weight of evidence (WOE) scheme developed by the EPA[14]. The WOE classifications of A, B1, B2, C-B2[15], and C are represented by mathematically equivalent intervals, A = 3/3, B = 2/3 and C = 1/3. The B2 category was considered the lower limit of the A-B interval and the value for B1 was assigned an average value between A and B. The WOE value for the C-B2[15] category was also derived by assigning an average value for the B-C interval. Hence the numerical WOE values were assigned: 1.00, 0.84, 0.67, 0.51 and 0.34, respectively. Class D and E compounds generally do not possess cancer potency factors and are assigned a value of 0. The complete algorithm is presented in Appendix B.

The oral carcinogen dose (d) is calculated at a reference risk of 1×10^{-4}, by solving the equation used to derive the q_1^* values. Thus,

$$risk = 1 - e^{-q_1^* d_c}$$

where

q = carcinogenic potency factor
d_c = carcinogenic dose
$risk$ = 1×10^{-4} as the reference risk value.

Noncarcinogenic dose is expressed as the oral reference dose (RfD) equivalent to a hazard index of 1. Thus,

$$dose_{nc} = RfD$$

where

$dose_{nc}$ = noncarcinogenic dose
RfD = oral reference dose at hazard index = 1

Dose units for both carcinogenic and noncarcinogenic scales are converted from per mg/(kg/day) and mg/kg/d to mg/d by dividing or multiplying by 70 kg, respectively.

If a compound possesses both noncarcinogenic and carcinogenic toxicity factors, the total dose is calculated according to the following equation:
where

$$Dose_T = \frac{1}{\left(\frac{1}{dose_{NC}}\right)+\left(\frac{1}{dose_C}\right)}$$

$Dose_T$ = Total Chronic Dose
$Dose_{NC}$ = Noncarcinogenic Dose
$Dose_C$ = Carcinogenic Dose

For the purpose of equivalent comparisons, all toxicity factors are expressed in terms of dose and as a result, a constant dose-based toxicity factor is calculated for each compound listed in the IRIS database.

The TRI chemical releases are converted from the units lb/yr to mg/d to correspond to the calculated dose units of mg/d using the following conversion factors:

1 year	= 365 days
1 lb chemical	= 0.435 kg chemical
1 kg chemical	= 1×10^6 mg chemical

The TRI release (mg/d) for each compound is divided by the calculated chronic $dose_T$ (mg/d). The resultant values (Chronic Indices) are ranked and target chemicals are identified which simultaneously account for both carcinogenic and noncarcinogenic toxicity. It is important to note that Single Component Indices (i.e. noncarcinogenic or carcinogenic) may also be calculated and ranked to identify target chemicals for specific endpoints of concern[16]. Those chemicals which do not possess primary or secondary toxicity factors are evaluated as residual releases and are ranked according to the mass released for each TRI category.

3.2. Facility Targeting: LOTUS spreadsheets which utilize the Chronic Index to identify specific facilities have also been developed. For example, the analysis may include a ranked list of facilities responsible for the highest toxic releases indicated by their Chronic Indices. The total releases for these chemicals in each geographic entity (i.e. county, zipcode zone, census tract, etc.) are summed, ranked and those facilities estimated to have the largest contribution to each entity's emissions may be identified. These facilities may also be characterized by related data including SIC codes and descriptions, parent company names, and participation in the 33/50 program[17].

EPA'S 33/50 Program targets 17 priority toxic pollutants and asks industry nationwide to voluntarily reduce releases of these chemicals 33% by the end of 1992 and 50% by the end of 1995. While these are national goals, each company selects its own individual reduction goals. The Program is multi-media and advocates pollution prevention (source reduction) as the preferred method for reducing releases.

4. LIMITATIONS

4.1. Dataset reconciliation: Several discrepancies were noted in reconciling the two datasets, IRIS and the EPCRA chemical list. EPCRA allows reporting of chemical classes as well as individual chemicals. Thus, most metals are reported both as elements and compounds, e.g. manganese or manganese compounds. The chemical nature of the "compound" is not specified according to EPCRA. Since IRIS provides toxicity information for specific compounds or elements, the information which corresponds to the generalized EPCRA reported releases for metals do not coincide. Thus, in order to maximize the data useability from both databases, metals which are reported on TRI as either elements or compounds are summed and assigned the toxicity factor available in IRIS.

While this approach may tend to overestimate the Chronic Index of some reported metal releases, it is consistent with the purposes described above. Both enforcement and planning activities can use this information as a screening tool to assist in determining the need for action. Should the decision to take action arise, then other sources of data should be investigated in depth to obtain more realistic estimates.

4.2. Valence State: Compounds which exist in more than one valence state, e.g. chromium (Cr) or arsenic (As) are particularly problematic. In the case of chromium, for example, IRIS possesses specific toxicity factors for Cr(III) and Cr(VI), but EPCRA only requires general reporting of Cr releases as chromium or chromium compounds. Thus, the TRI database does not distinguish between releases of the less toxic Cr(III) and the more toxic Cr(VI). In order to develop a conservative estimate of the Chronic Index, the toxicity factor for the more toxic compound is used in the calculation. This limitation should be considered in evaluating the effectiveness of this approach for certain media.

4.3. Exposure route: While oral exposure resulting from soil deposition of air emissions may constitute the primary route of chemical exposure for some types of industrial sources[16], the direct inhalation route may contribute to exposure to air emissions from other source types. This exposure concept would argue for the inclusion of inhalation rather than oral toxicity data. However, because many TRI compounds do not possess inhalation toxicity data (RfC) for noncancer endpoints, some other value, such as an oral RfD, would be required as a default for missing inhalation values. The combination of data from two exposure routes may result in an inordinate weighting of those chemicals which possess inhalation RfCs compared to those which are represented by oral RfDs. Thus, the usefulness of the resultant Index as representative of TRI releases and as a comparative indicator is limited. Further study will include a distributional comparison of existing RfCs and RfDs to determine the existence of differences in relative toxicity between the two routes of exposure.

4.4. Bioavailability (food/water): The relative toxicity of some compounds depends on the vehicle of ingestion, i.e. food or water and toxicity values may be listed separately on the IRIS database. Generally, compounds present in water are more bioavailable and more toxic when ingested with water. In order to provide some measure of consistency, if two values are reported in IRIS, the drinking water oral toxicity factor is used to calculate the Index.

4.5. Standard Dose Scale: The methodology presented in this analysis assumes acceptance of the current RfD and CRAVE workgroup processes. While each process contains elements of uncertainty which stem both from subjective judgements and calculated mathematical error, the resultant Chronic Index scale merely compares one Index value to another. Thus, errors inherent in the approval processes are less likely to influence the results of the Chronic Index ranking. As these accepted processes are refined[18,20,21], the Index method will adopt the outputs of the new procedures.

5. CONCLUSION

As with all systems which attempt to utilize imperfect data to achieve conclusions, this system also possesses its contingent of limitations. When utilizing of results of this process, it is incumbent upon the user that the information is applied in the context of these limitations.

Despite its limitations, this approach provides a current best-science approach to support ongoing decision-making processes. Moreover, since the method assigns a constant toxicity factor to each chemical, it permits tracking of the toxicity reductions in releases reported for individual chemicals or facilities from year to year. The method also allows for inclusion of new information as it becomes available, both in terms of toxicity and governmental regulations.

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For additional information, (215) 597-3175.

Approved by: _____

Thomas J. Maslany, Director
Air, Radiation and Toxics Division

Appendix A

Carcinogenic Hazard Index Calculation: The quantitative relationship between the noncarcinogenic and carcinogenic scales may be described by individually ranking the two scales and comparing the values at designated scale points such as percentiles.

Based on policy issues discussed in Section 2.3, reference points denoting acceptable limits for the purpose of hazard identification are established at a risk level of 1 x 10^{-4} for carcinogens and a hazard index of 1 for noncarcinogens. Using the approach outlined in Section 3.1, doses are calculated for each scale and the resultant dose values are rank ordered from most toxic (lowest acceptable dose) to least toxic (highest acceptable dose). The order statistic for percentiles 1-99 are calculated for both the ranked carcinogenic dose scale and the ranked noncarcinogenic dose scale, as (n+1)p/100 where n= number of observations and p= percentile[1] and the value corresponding to each order statistic is recorded. The ratio of carcinogenic dose to noncarcinogenic dose at each percentile expresses the differences in magnitude at regular scale intervals as shown in Figure A.1.

An example of the hazard index equivalent to 1 x 10^{-4} risk may be calculated using the 50th percentile. The hazard equal to a carcinogenic risk of 1 x 10^{-4} may be calculated as

$$\text{Carcinogenic Hazard} = \frac{(\text{reference hazard} \times \text{percentile}_C)}{\text{percentile}_{NC}}$$

where

percentile_C = 50th percentile of carcinogen doses at reference risk
percentile_{NC} = 50th percentile of noncarcinogenic doses at reference hazard
reference hazard = 1

The ratio of percentiles from the carcinogenic and noncarcinogenic data using both IRIS and HEAST values[2], suggests that carcinogenic hazard is more restrictive than noncarcinogenic hazard in a ratio of about 0.04:1, or 25 fold. Figure A.1. shows a scatterplot of the scale ratios.

Figure A.1.: Scatterplot of Dose Ratio values

[1] *Snedecor, G.W. and Cochran W.G. (1976) Statistical Methods, 6th Ed., Iowa State University Press, Ames, Iowa.*

[2] *Data from the IRIS database constitutes a subset of the combined HEAST/IRIS dataset and while the median values may vary, the calculation of relative emphasis is similar.*

Table A.1. below shows the mean +/- 95% confidence limits for this data. It is important to emphasize that the relative emphasis employed by this methodology does not imply biological significance regarding severity of effect. Instead, it provides a mechanism for assessing chronic toxic effects within the confines of Agency policy with regard to regulations concerning carcinogens and noncarcinogens[4,9].

The following analysis describes the relative emphasis of carcinogens and noncarcinogens according to Agency policy statements for the entire percentile distribution of dose ratios shown in Figure A.1. Those ratios occurring at the extremes of the percentile distribution, i.e. greater than the 75th percentile (Quartile 4) or less than the 25th percentile (Quartile 1) exhibited the greatest variability. Dose ratios calculated for values between the 25th and 75th percentiles (Quartiles 2 and 3) demonstrated good agreement.

Table A.1: Descriptive Statistics for CPF:RfD quartiles

Quartile	N	Mean of Dose Ratios (+/-95% CI)	S.E.M.	Variance σ^2	Correlation r^2	p-value
1	25	97.8 (4, 192)	45.5	51716.9	0.21	0.023
2	25	29.2 (27, 31)	1.1	28.1	0.68	<0.001
3	25	16.7 (15, 18)	0.8	16.1	0.68	<0.001
4	24	15.2 (12, 19)	1.7	71.4	0.30	0.006
2 and 3	**50**	**23.0 (21,25)**	**1.1**	**61.1**	**0.88**	**<0.001**
1,2,3 and 4	**99**	**23.9 (22, 26)**	**1.1**	**118.8**	**0.57**	**<0.001**

Appendix B: Chronic Index Algorithm

$$\textit{Chronic Index} = \left[\frac{\dfrac{mass \times kg/lb \times mg/kg}{d/yr}}{\left[\dfrac{1}{\dfrac{1}{\left[\dfrac{\ln(1-risk)}{-CPF_o} \times WOE \right] \times bw} + \dfrac{1}{\dfrac{RfD}{bw}}} \right]} \right]$$

where

mass = TRI mass (lb/yr)
risk = 1×10^{-4} = reference risk
WOE = carcinogenic weight of evidence
CPF_o = oral cancer potency factor $(mg/kg/day)^{-1}$
RfD = oral reference dose (mg/kg/day)
bw = body weight (70 kg)
d/yr = 365 = (conversion factor)
mg/kg = 1,000,000 = (conversion factor)
kg/lb = 0.453 = (conversion factor)