

## Hierarchy of Toxicological Information

### Issue

Should Ecology revise the hierarchy of information sources for toxicological parameters (cancer slope factors and reference doses) currently included in the MTCA cleanup rule?

### Background

The MTCA cleanup level equations require information on the toxicological properties of each hazardous substance. There are many sources of toxicological information and the MTCA cleanup regulation establishes a general hierarchy or preferences for toxicological information. For example, WAC 173-340-708(8) states that cleanup levels must be calculated using carcinogenic potency factors (cancer slope factors) published by EPA in the Integrated Risk Information System (IRIS) database. The IRIS values must be used unless there is clear and convincing evidence that such values are inappropriate. The current rule also states that cancer slope factors published by EPA in the Health Effects Assessment Summary Table (HEAST) or developed by the National Center for Environmental Assessment (NCEA) can be used when values are not available in the IRIS database. The MTCA rule includes similar criteria for selecting toxicity parameters based non-cancer health risks (See WAC 173-340-708(7).

There have been several scientific and regulatory developments since the 2001 rule revisions. These include the following:

- EPA Guidelines on Toxicity Parameters: In 2003, the EPA's Office of Solid Waste and Emergency Response (OSWER) issued Directive 9285.7-53, which provides recommended sources of toxicity data for developing screening levels for various media and conducting site-specific human health risk assessments.<sup>1</sup> The hierarchy of toxicity information recommended by OSWER Directive 9285.7-53 is:
  - Tier 1 – EPA's Integrated Risk Information System (IRIS)
  - Tier 2 – EPA's Provisional Peer Reviewed Toxicity Values (PPRTVs)
  - Tier 3 – Other (California EPA, ATSDR, HEAST)
- Health Effects Assessment Summary Tables (HEAST): Shortly after the 2001 rule revisions, EPA decided to stop updating the HEAST values. Consequently, many HEAST values are now inconsistent with more recent scientific studies and regulatory guidance. For example, many of the inhalation toxicity values in HEAST were developed by using simple route-to-route extrapolation methods. This is inconsistent with current EPA guidance.<sup>2</sup>

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<sup>1</sup> USEPA. 2003. *Human Health Toxicity Values in Superfund Risk Assessment*. Office of Solid Waste and Emergency Response, Washington, D.C. Publication 9285.7-53. <http://rais.ornl.gov/homepage/hhmemo.pdf>.

<sup>2</sup> USEPA. 2009. *Risk Assessment Guidance for Superfund. Volume I: Part F, Supplemental Guidance for Inhalation Risk Assessment*. Office of Superfund Remediation & Tech. Innovation. Washington D.C. EPA-540-R-070-002. In this guidance, EPA recommends that risk assessors not use inhalation toxicity values generated using simple route-to-route extrapolation.

- Regional Screening Tables: Several EPA regional offices and the Oak Ridge National Laboratory maintain the “Regional Screening Levels for Chemical Contaminants at Superfund Sites” which serves as source of toxicity parameters. This information is published on a website maintained by the Oakridge National Laboratory under an interagency agreement with EPA. The national lab works with EPA to update the website on a bi-annual basis. EPA uses the following data hierarchy (based OSWER Directive 9285.7-53) on for the Regional Screening Tables:
  - EPA’s Integrated Risk Information System (IRIS).
  - The Provisional Peer Reviewed Toxicity Values (PPTRVs) derived by EPA’s Superfund Health Risk Technical Support Center (STSC).
  - The Minimal Risk Levels (MRLs) developed by the Agency for Toxic Substances and Disease Registry (ATSDR).
  - The California Environmental Protection Agency (OEHHA) Office of Environmental Health Hazard Assessment’s Chronic Reference Exposure Levels from December 18, 2008 and the Cancer Potency Values from December 17, 2008.
  - Screening toxicity values in an appendix to certain PPRTV assessments.<sup>3</sup>
  - Health Effects Assessment Summary Table (HEAST) toxicity values.

### **MTCA Rulemaking Options**

Ecology has reviewed the new scientific and regulatory information and believes it is appropriate to consider revisions to the toxicological information hierarchy in the MTCA cleanup regulation. Ecology has considered two main options for resolving this rulemaking issue:

1. No Revision. Under this option, Ecology would not revise the MTCA cleanup regulation provisions that establish the hierarchy of toxicological information sources.
2. Revisions to Reflect Current Information Sources: Under this option, Ecology would revise WAC 173-340-708(7) and (8) to reflect current EPA guidance and information sources used by other state and federal cleanup programs.

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<sup>3</sup> EPA includes the following statement on the RST webpage: “While we have less confidence in a screening toxicity value than in a PPRTV, we put these ahead of HEAST toxicity values because these appendix screening toxicity values are more recent and use current EPA methodologies in the derivation, and because the PPRTV appendix screening toxicity values also receive external peer review”

## Draft Revisions and Rationale

Ecology plans to revise the MTCA toxicological information hierarchy to reflect current information sources used by state and federal agencies (Option 2). A draft of the proposed revisions is shown below.

### **Draft Rule Provisions on Cancer Slope Factor Hierarchy and Information Updates WAC 173-340-708(8)**

#### **(8) Cancer slope factor and inhalation unit risk factors.**

(a) Cancer slope factors and inhalation unit risk factors available through the integrated risk information systems (IRIS) data base be used to establish cleanup levels and remediation levels. If such values are not available through the IRIS database, cancer slope factors and inhalation unit risk factors available from the National Center for Environmental Assessment shall be used. These values shall be used unless the department determines that there is clear and convincing scientific data which demonstrates that the use of a particular value is inappropriate.

(b) Cancer slope factors and inhalation unit risk factors from other sources may be used to establish cleanup levels and remediation levels when values are not available in the IRIS database. The department will use the criteria in OSWER Directive 9285.7-53 when evaluating whether particular values can be used to support decisions on cleanup levels or remediation levels.

(c) The department shall publish and periodically update a list of cancer slope factors and inhalation unit risk factors. The department shall provide an opportunity for public review and comment before publishing a final list and/or updated list.

Ecology's rationale for the draft revision includes the following:

- This draft revision is consistent with the EPA data hierarchy used to support decisions at federal Superfund sites and complies with the MTCA statutory directives. The EPA Superfund program uses the EPA data hierarchy<sup>4</sup> to support decisions at cleanup sites. The EPA data hierarchy also provides the foundation for updates to the Regional Screening Tables. Consequently, this option promotes consistency with the federal Superfund program and helps to ensure that MTCA cleanup standards will be "...at least as stringent as the cleanup standards under section 121 of the federal cleanup law, 42 U.S.C. Sec. 9621, and at least as stringent as all applicable state and federal laws, including health-based standards under state and federal law..."
- This draft revision will allow more timely use of high quality scientific information to support MTCA decision-making. The current rule provision is based on EPA performing regular reviews of new scientific information. However, resource limitations and interagency review processes have delayed numerous EPA reviews. This was highlighted by the General Accounting Office (GAO) in their review of EPA's process for performing chemical assessments. They concluded:

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<sup>4</sup> USEPA. 2003. *Human Health Toxicity Values in Superfund Risk Assessment*. Office of Solid Waste and Emergency Response, Washington, D.C. Publication 9285.7-53. <http://rais.onrl.gov/homepage/hhmemo.pdf>.

*...EPA has not been able to routinely complete credible assessments or decrease its backlog of ongoing assessments. Several key factors have contributed to EPA's inability to achieve a level of productivity that is needed to sustain the IRIS program and database, including the OMB/interagency review process managed by OMB, certain management decisions and issues regarding the IRIS program, and the compounding effects of delays. In addition, because the OMB/interagency review process is not transparent, this change also limits the credibility of IRIS assessments. (GAO, 2008, p.11)<sup>5</sup>*

- This draft revision is consistent with approaches being used by other state agencies and the Department of Defense. Many states use the EPA data hierarchy (see guidance materials prepared by New Hampshire<sup>6</sup> and Oregon<sup>7</sup>) or variations on the EPA hierarchy (New Jersey<sup>8</sup>) to support regulatory decisions. The Department of Defense has also adopted policies that are consistent with the EPA data hierarchy.<sup>9</sup>
- This draft revision provides a workable and transparent approach for integrating new scientific information into the MTCA decision-making process.
- There appears to be general support for the revised approach among advisory members: Ecology asked members of the MTCA/SMS Advisory Group and the Vapor Workgroup to

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<sup>5</sup> General Accounting Office. 2008. Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Risk Information System. Report to the Chairman, Committee on Environment and Public Works, U.S. Senate. GAO-08-440.

<sup>6</sup> The New Hampshire vapor intrusion guidance (p. 37) includes the following:

“In 2003, the EPA's Office of Solid Waste and Emergency Response (OSWER) issued Directive 9285.7-53, which provides recommended sources of toxicity data for developing screening levels for various media and conducting site-specific human health risk assessments. The hierarchy of toxicity information recommended by OSWER Directive 9285.7-53 is:

- Tier 1– EPA's Integrated Risk Information System (IRIS)
- Tier 2 – EPA's Provisional Peer Reviewed Toxicity Values (PPRTVs)
- Tier 3 – Other (CAL EPA, ATSDR, HEAST)

The EPA's IRIS database is the generally preferred source of URi and RfCs for evaluating inhalation exposure. The PPRTVs are provisional toxicity values recommended by EPA's National Center for Environmental Assessment (NCEA). PPRTVs are the second recommended tier of toxicity values; however, EPA has restricted access to this database. When IRIS values were not available EHP consulted EPA Region 9's Preliminary Remediation Goals (PRG) table, which contains the latest recommended toxicity factors according to the OSWER directive. Please note that the toxicity values identified on IRIS are frequently updated. It is incumbent upon the users of this guidance to check IRIS and EPA Region 9's PRG Table to verify that the most current toxicity information is being when completing site-specific human health risk assessments.”

<sup>7</sup> <http://www.deq.state.or.us/lq/rbdrm.htm>

<sup>8</sup> [http://www.nj.gov/dep/srp/regs/rs/bb\\_ingest\\_dermal.pdf](http://www.nj.gov/dep/srp/regs/rs/bb_ingest_dermal.pdf)

<sup>9</sup> Department of Defense. 2007. Identification and Selection of Toxicity Values/Criteria for CERCLA and Hazardous Waste Site Risk Assessments in the Absence of IRIS Values. Attachment 1 to memorandum “Actions in Response to Perchlorate Releases” From Alex A. Beehler (Assistant Deputy Under Secretary of Defense) to Deputy Assistant Secretary of the Army (Environment, Safety and Occupational Health), Deputy Assistant Secretary of the Navy (Environment) and Deputy Assistant Secretary of the Air Force (Environment, Safety and Occupational Health). September 21, 2007.

review and provide comments on the toxicological data hierarchy. (A summary of comments on this issue is provided later in this section.) There appears to be general agreement on several points:

- Ecology should continue to rely on the IRIS database and NCEA toxicity values (PPTRVs) as the primary bases for cleanup level development.
- Ecology should reduce its reliance on the HEAST database because EPA no longer updates these values.<sup>10</sup>
- Ecology should provide regular updates to the Cleanup Levels and Risk Calculations (CLARC) database to incorporate new toxicity values. Ecology believes this should be a transparent process. We believe it makes sense to automatically update the CLARC database when EPA publishes a final IRIS value. We also believe that it is appropriate for the public to have an opportunity to review and comment on proposed updates not based on new IRIS or PPRTV values.

Ecology believes it will continue to be necessary to supplement the IRIS/PPRTV values with toxicity values from other sources. Decisions on the use of these values will be made when updating the CLARC database. Members provided a wide range of opinions on the use of other toxicity values (California EPA, ATSDR<sup>11</sup>, etc.) when IRIS and PPRTV values are not available.

- Use of Draft Toxicity Values: Several reviewers recommended that cleanup levels should not be established using draft toxicity values that are undergoing scientific and/or public review. Ecology agrees that draft toxicity values are generally not an appropriate basis for establishing cleanup levels/screening levels.<sup>12</sup>
- Use of ATSDR Minimal Risk Levels (MRLs): One reviewer suggested that MRLs may be an appropriate basis for establishing cleanup levels. Ecology agrees that MRLs developed by ATSDR provide a credible basis for calculating cleanup levels. The ATSDR methods are similar to those used by EPA to develop oral reference doses and reference concentrations. ATSDR procedures for establishing MRLs include extensive peer review and opportunity for public review and comment. However, the practical impact on cleanup levels is unclear. Very few of the screening levels in the EPA Regional Screening Tables are derived using MRLs.

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<sup>10</sup> EPA has stopped updating the HEAST database and, consequently, many values are out-of-date and/or inconsistent with current EPA guidance. However, the HEAST values for some chemicals remain consistent with current scientific information.

<sup>11</sup> ATSDR publishes toxicological profiles for hazardous substances found at federal Superfund sites. When preparing these documents, ATSDR publishes Minimal Risk Levels (MRLs) that are developed using procedures that are virtually identical to the EPA methods for establishing reference doses. However, the ATSDR website includes the following qualifier "It is important to note that MRLs are not intended to define cleanup or action levels for ATSDR or other Agencies..."

<sup>12</sup> OSWER Directive 9285.7-53 states that "In general, draft toxicity assessments are not appropriate for use until they have been through peer review, the peer review comments have been addressed in a revised draft, and the revised draft is publicly available."

- Use of California EPA Toxicity Values: Several members expressed concerns about using toxicity values developed by the California EPA to establish MTCA cleanup levels. Members identified two main concerns:
  1. Peer Review and Transparency: Several members expressed concerns about the level of peer review and opportunity for public comment provided by the California EPA. Ecology has reviewed those procedures. While not equivalent to the methods used by EPA to develop IRIS toxicity values, the California EPA procedures include independent scientific reviews and opportunities for public review and comment on draft values. Similar to the EPA IRIS process, the California EPA evaluates scientific peer review and public comments before developing final toxicity values. When developing the EPA data hierarchy, EPA pointed to the California process as an example of a transparent process with opportunities for external review.
  2. Technical Methods: Several members questioned whether the California EPA method for establishing toxicity values is consistent with current scientific information and EPA regulatory guidance. We have reviewed the methods used by the two agencies. With few exceptions, the California EPA methods are very similar to the EPA methods.

Ecology performed two evaluations designed to evaluate the practical implications of using the California EPA values. First, we evaluated how frequently the California EPA toxicity values might be used to establish MTCA cleanup levels. This was done by reviewing the Regional Screening Tables to identify the cancer slope factors and inhalation unit risk factors for the 50 chemicals meeting the draft MTCA definition for carcinogen (see previous section). The results of that evaluation are summarized in the table below.

<b>Toxicity Values Used to Develop Regional Screening Concentrations Based on Cancer Risks for the 50 Carcinogens Among the 100 Highest Ranked Substances on the 2007 CERCLA Priority List</b>		
Source of Toxicity Value in Regional Screening Tables	Oral Cancer Slope Factor	Inhalation Unit Risk Factor
Integrated Risk Information System (IRIS)	34	25
Provisional Peer Reviewed Toxicity Values (PPRTV)	1	2
California Environmental Protection Agency	5	17
Health Effects Assessment Summary Tables (HEAST)		
Other	1	0
No Value Available	7	6

Ecology has also evaluated the reasons for the use of the California EPA values and the potential impacts associated with greater reliance on those values. The results of that evaluation are shown below. There appear to be three main reasons for the use of IUR values developed by the California EPA: (1) the California EPA value replaces an out-of-date HEAST value; (2) the California EPA value replaces an inhalation value that is based on direct extrapolation from an oral cancer slope factor; and (3) no other values are available. As shown in the table below, the California EPA values tend to be slightly less stringent than values obtained from HEAST or derived by direct extrapolation from an oral slope factor.

Substance	Current MTCA inhalation cancer potency factor	Basis	Inhalation Unit Risk Factor (from MTCA CPFi)	California EPA Inhalation Unit Risk Factor
Benzo[a]pyrene (multiple PAHs)	6.1 (mg/kg/day) <sup>-1</sup>	HEAST	1.7E-03 (ug/m <sup>3</sup> ) <sup>-1</sup>	1.1E-03 (ug/m <sup>3</sup> ) <sup>-1</sup>
Trichloroethylene	0.089	HEAST/CLARC	2E-06	2E-06
Tetrachloroethylene	0.021	HEAST/CLARC	5.9E-06	5.9E-06
Nickel	1.7	HEAST	4.9E-04	2.6E-04
TCDD	150,000	HEAST/Oral	4.3E+01	3.8E+01
PCBs	2	Oral slope factor	5.7E-04	5.7E-04
DDD	0.24	Oral slope factor	6.9E-05	6.9E-05
Pentachlorophenol	0.12	Oral slope factor	3.4E-05	5.1E-06
DEHP	0.014	Oral slope factor	4E-06	2.4E-06
3,3'-Dichlorobenzidine	0.45	Oral slope factor	1.3E-04	3.4E-06

Ecology has also evaluated how toxicity values developed by California EPA compare with toxicity values developed by the Environmental Protection Agency. This was done by downloading the oral slope factors included in the IRIS database and comparing those values to oral cancer slope factors developed by the California EPA. The IRIS database currently includes 88 oral cancer slope factors for 78 chemicals. The California EPA has developed oral cancer slope factors for 60 of those 78 chemicals. **NOTE: This evaluation differs from the earlier comparison because the 78 chemicals include ones that are not found or rarely found at Superfund sites.**

In general, the California EPA oral slope factors are similar (but slightly higher) than the EPA values for the same chemical. Ecology recognizes that this comparison is somewhat simplistic in that it does not consider when the different values were developed, the basis for different values, etc. However, the comparison reinforces our general conclusion that the California EPA values are consistent with current scientific information and federal risk assessment policies and procedures.

Summary of Comparison of Cancer Slope Factors in the Integrated Risk Information System and the California Environmental Protection Agency Toxicity Criteria Database	
Range of Cancer Slope Factor Ratios (CalEPA CSF/USEPA CSF)	Number of Chemicals
Chemicals with slope factor ratio greater than 3	4
Chemicals with slope factor ratio between 2 and 3	10
Chemicals with slope factor ratio between 1 and 2	15
Chemicals with the same cancer slope factor (ratio = 1)	18
Chemicals with slope factor ratio between 0.5 and 1	6
Chemicals with slope factor ratio less than 0.5	7
Average Slope Factor Ratio (60 chemicals)	1.6

Comments on Draft Revisions to MTCA Toxicological Hierarchy [Note: Most comments have been summarized to conserve space].	
	Comment
Comments (verbal) made during the March 2010 MTCA/SMS Advisory Group Meeting	<p>Use EPA's toxicity review process that's well established and has gone through public peer review, e.g. IRIS.</p> <p>Don't just arbitrarily "pick up" toxicity values from other sources.</p> <p>Toxicity information tends to be in a state of flux.</p> <p>You have to be really careful about where you draw your values, sources, references, etc.</p>
Patty Boyden/Mike Stoner	<p>EPA's IRIS database has been recognized as the "gold standard" for toxicological data due to its rigorous external peer review process for data inclusion. Ecology should continue to rely on IRIS as the primary source of data for cleanup level development.</p> <p>The use of RSTs is discouraged because of the lack of standardization. As noted by the Science Panel, the use of RSTs would require Ecology to develop a process of external peer-review prior to MTCA use. Such a process would use State resources to duplicate EPA's efforts to update IRIS and is therefore not recommended.</p>
Larry Dunn	<p>On the hierarchy of toxicological information, IRIS is indeed the gold standard but as noted is a lengthy process to complete. Regional screening tables are reasonable to use for a basis to update the CLARC data base. Annual updates should be sufficient unless an emerging issue is identified with a new chemical.</p>
Chris Waldron	<p>A systematic and regular update of toxicity values should be implemented for all toxicity values on CLARC.</p> <p>(1) The use of provisional toxicity values that have not undergone external peer review is a significant concern because of the high degree of uncertainty. Ecology should establish a hierarchy of sources of peer-reviewed toxicity values. There have been many instances (e.g., trichloroethylene toxicity values) where project managers at Ecology have required the use of draft or provisional toxicity values on projects – which have then changed. This is costly and unnecessary.</p> <p>(2) The language in Figure 1 (8)(b) – 2<sup>nd</sup> sentence is vague (i.e., "and other credible sources"). Ecology should identify "other credible sources" here in order to eliminate confusion. I do not think that Ecology's goal or mission should be to perform toxicity assessments and develop toxicity values from toxicity studies. This would duplicate the work being performed by the EPA.</p>
Mike Ehlebracht	<p>Ecology's approach makes sense to me. I use the on-line CLARC database fairly frequently and think it is a great tool.</p>
Neil Morton	<p>I think the "hierarchy" included proposed by Ecology is too vague. If the intention of Ecology is to follow the EPA 2003 hierarchy, which I think makes sense, then this should be stated. Especially since the EPA Regional Screening Table values were calculated using toxicity values obtained following EPA's 2003 hierarchy.</p>
Priscilla Tomlinson	<p>I consider that MTCA hierarchy to be outdated and recommend that it be changed, but not as shown in Figure 1. First, I recommend reversing the order of HEAST and NCEA (PPRTV) in the hierarchy, because HEAST has become so outdated, so the hierarchy would be IRIS, NCEA, HEAST. Second, I recommend using CalEPA and EPA Region 3 PRG table toxicity values only after evaluating them to verify that they have undergone</p>

	<p>sufficient peer review. My own experience reviewing one CalEPA toxicity value, and what I have heard from others about some of the EPA Region 3 table values, makes me inclined not to trust them without checking into their derivation. Another potential source of toxicity data is ATSDR's minimal risk levels, but I'm not familiar with their peer review process. I would be willing to investigate the ATSDR peer review process to assist you in decision making when I return from my vacation. One option for using toxicity values that are not considered as trustworthy as the IRIS/NCEA/HEAST list, either because they have undergone insufficient peer review or because their peer review status cannot be verified, would be to use them only for screening purposes to eliminate a chemical from further consideration but not to use them for establishing CULs. However this approach would add an additional layer of complexity to the process and might be difficult to implement.</p>
<p>Barbara Trejo</p>	<p>A systematic update process is necessary. However, the update should occur more frequently than annually if significant changes in toxicity values occur. This would help ensure that the regulated community is using the appropriate values</p> <p>Not having reviewed the various toxicity values it is not possible to comment other than stating that IRIS or Regional Screening Tables values generally undergo extensive peer review before being adopted. We suggest that Ecology modify the proposed WAC 173-340-708 language, below, as noted.</p> <p>According to the information noted above and below, IRIS, Regional Screening Tables, petroleum fraction sources and other credible sources would be used. Section 8(a) should be revised to reflect that fact.</p> <p>Suggest including the reference for developing non-carcinogenic toxicity values.</p>
<p>MTCA Science Panel March 25, 2010</p>	<p>Regional Screening Tables (RST) may be a reasonable source of toxicity values. However, the tables include toxicity values from several different sources with varying degrees of scientific peer review. Panel is not familiar enough with tables to provide a generic answer.</p> <p>Panel appeared to be supportive of using the RST values as a starting point for updating MTCA cleanup levels. However, the rationale for updates needs to reflect more than the fact that a particular toxicity values appears in the RST.</p> <p>Internal peer review within EPA is not equivalent to the external peer review used for IRIS updates. Panel was unclear on RST review process.</p> <p>Panel appeared to support some type of external review process surrounding the use of some or all RST values prior to use under MTCA. They thought that once-a-year updates were sufficient. In terms of mid-year changes, they thought that changes less than an order of magnitude could wait for annual updates.</p> <p>HEAST should not be used as a general reference. However, some HEAST values may still reflect current science on particular chemicals.</p>

