DEPARTMENT OF
ECOLOGY
State of Washington

Revisions to MTCA Cleanup Regulation Key Definitions

Prepared for the MTCA Science Advisory Board (SAB) Discussion on June 2, 2008

By

Washington State Department of Ecology
Toxics Cleanup Program

Table of Contents

Introduction……..5

Summary

Background

Relationship Between June 2nd Issues and Overall Rule Process

Organization of Document

Definition of "Averaging Time"……...9

Definition of "Bioaccumulation Factor" (BAF)……13

Definition of "Carcinogen"……19

Introduction

Summary

Ecology plans to review and revise the Model Toxics Control Act (MTCA) Cleanup Regulation and the cleanup provisions in the Sediment Management Standards (SMS) rule. The Toxics Cleanup Program (TCP) has developed an initial list of rulemaking issues (See below). TCP is developing a rule plan and schedule.

Over the next eighteen months, TCP plans to consult with the Science Advisory Board (SAB) on many of these issues. For the June 2008 Board meeting, TCP has identified several initial issues. These initial issues focus on the regulatory definitions for key terms used in one or both of the two rules. These include new or revised terms:

- Averaging time
- Bioaccumulation Factor (BAF)
- Carcinogen.

Background

The Model Toxics Control Act (MTCA) Cleanup Regulation is the state's primary tool for cleaning up hazardous waste sites. The Sediment Management Standards (SMS) rule is the state's primary tool for managing contaminated sediments. Over the past six months, the Toxics Cleanup Program (TCP) has held scoping meetings to identify rule-related concerns and issues. Based on these meetings, TCP plans to review and revise the MTCA rule and cleanup provisions in the SMS rule. The main purpose of this rule revision is to:

- Set clear policies and methods for sediment cleanup actions (for example, integrating the MTCA and SMS rule requirements for cleanup standards of bioaccumulative chemicals).
- Revise and update cleanup requirements to reflect new scientific information and revisions to state and federal regulations (for example, reviewing new information on the health risks associated with blood lead levels below10 ug/dL).
- Revise cleanup requirements to address implementation concerns identified since the 2001 rule amendments (for example, provisions for property-specific opinions under TCP's Voluntary Cleanup Program).
- Revise the MTCA rule to incorporate new statutory requirements (for example, the Uniform Environmental Covenants Act passed by the Washington Legislature in 2007).

Relationship Between June 2006 Issues and Overall Rulemaking Process

In early May 2008, Ecology's Director approved TCP's proposal to revise the MTCA and SMS rules. TCP is developing a final issue list and preparing a rule plan and schedule. The rule plan

will describe the processes that TCP will use to prepare the rule revisions (including processes for SAB and stakeholder involvement).

The three definitions in this discussion paper are among the longer list of rulemaking issues being developed by TCP. TCP recognizes that each term is used within the MTCA decision-making process. TCP anticipates that further discussion will needed on the implications of the revised definitions when reviewing the procedures for establishing cleanup standards and selecting cleanup actions.

Organization of the Review Materials

Ecology believes that several regulatory definitions in the MTCA rule need to be updated based on new scientific information and/or regulatory requirements. Table 1 summarizes the current definitions and the draft revisions developed by Ecology.

The discussion materials are divided into three sections that correspond to the three regulatory definitions being reviewed by Ecology. Each section includes:

- Question for the Science Advisory Board: This part identifies one or more questions related to each regulatory definition.
- Background: This part summarizes the current rule definition and how the term is used within the MTCA decision-making framework.
- Draft Definition: This part identifies the revised definition developed by Ecology.
- Rationale for Draft Definition: This part summarizes Ecology's rationale for the draft definition.

Table 1: Draft Revisions to Selected Definitions in the Model Toxics Control Act (MTCA) Cleanup Regulation		
Term	**Current Definition**	**Draft Revision**
Averaging Time **(Modifying an existing term)**	**"Averaging time"** means the time over which the exposure is averaged. For noncarcinogens, the averaging time typically equals the exposure duration. For carcinogens, the averaging time equals the life expectancy of a person.	**"Averaging time"** means the time over which the exposure is averaged. For noncarcinogens, the averaging time typically equals the exposure duration. For carcinogens, the averaging time typically equals 70 years or other values consistent with the assumptions used to develop the cancer slope factor ~~the life expectancy of a person~~.
Bioaccumulation Factor **(Adding a new term)**		**"Bioaccumulation factor"** or **"BAF"** means the ratio of the concentration of a hazardous substance in the tissue of an organism to its concentration in the medium of concern (for example soil, surface water, or sediment). The BAF takes into account both the direct exposure of the organism to the medium of concern and indirect exposure of the organism through ingestion of food sources that are exposed to the medium of concern.
Bioconcentration Factor **(Modifying an existing term)**	**"Bioconcentration factor"** means the ratio of the concentration of a hazardous substance in the tissue of an aquatic organism divided by the hazardous substance concentration in the ambient water in which the organism resides.	**"Bioconcentration factor"** or **"BCF"** means the ratio of the concentration of a hazardous substance in the tissue of an aquatic organism divided by the hazardous substance concentration in the ambient water in which the organism resides.
Biota Sediment Accumulation Factor **(Adding a new term)**		
Cancer Slope Factor **(Adding a new term to replace an existing term)**	**"Carcinogenic potency factor"** or **"CPF"** means the upper 95th percentile confidence limit of the slope of the dose-response curve and is expressed in units of (mg/kg-day)-1. When derived from human epidemiological data, the carcinogenic potency factor may be a maximum likelihood estimate.	**"Cancer slope factor"** or **"CSF"** means the upper 95th percentile confidence limit of the slope of the dose-response curve and is expressed in units of (mg/kg-day)-1. When derived from human epidemiological data, the cancer slope factor may be a maximum likelihood estimate.

Term	Current Definition	Draft Revision
Carcinogen **(Modifying an existing term)**	**"Carcinogen"** means any substance or agent that produces or tends to produce cancer in humans. For implementation of this chapter, the term carcinogen applies to substances on the United States Environmental Protection Agency lists of A (known human) and B (probable human) carcinogens, and any substance that causes a significant increased incidence of benign or malignant tumors in a single, well conducted animal bioassay, consistent with the weight of evidence approach specified in the United States Environmental Protection Agency's Guidelines for Carcinogen Risk Assessment as set forth in 51 FR 33992 et seq.	**"Carcinogen"** means any hazardous substance or group of hazardous substances that is known or suspected to increase the probability of developing cancer. For purposes of implementing this chapter, the term carcinogen applies to substances that have been identified as "carcinogenic to humans" or "likely to be carcinogenic to humans" by the Environmental Protection Agency, as a Group 1, 2A, or 2B carcinogen by the International Agency for Research on Cancer or as a "known to be a human carcinogen" or "reasonably anticipated to be a human carcinogen" by the National Toxicology Program.

Definition of Averaging Time (AT)

Question for Science Advisory Board

Is the draft definition consistent with current scientific information and the MTCA procedures used to calculate cleanup levels for carcinogens?

Background

The MTCA Cleanup Regulation includes methods and policies for establishing cleanup levels that are based on preventing human health risks resulting from exposure to hazardous substances. For example, the MTCA rule includes the following equation for establishing ground water cleanup levels based on preventing unacceptable cancer health risks.

Ground Water Cleanup Standards [Equation 720-2]

$$\text{Ground water cleanup level} = \frac{\text{RISK x ABW x AT x UCF}}{\text{CPF x DWIR x ED x INH x DWF}}$$

Where:

Risk	=	Acceptable cancer risk level (1 in 1,000,000) (unitless)
ABW	=	Average body weight during the exposure duration (70 kg)
AT	=	Averaging time (75 years)
UCF	=	Unit conversion factor (1,000 ug/mg)
CPF	=	Carcinogenic potency factor as specified in WAC 173-340-708(8) (kg-day/mg)
DWIR	=	Drinking water ingestion rate (2.0 liters/day)
ED	=	Exposure duration (30 years)
INH	=	Inhalation correction factor (use value of 2 for volatile organic compounds and 1 for all other substances [unitless])
DWF	=	Drinking water fraction (1.0) (unitless)

The averaging time is one of the parameters used to calculate cleanup levels. The MTCA rule includes the following definition:

> *"**Averaging time**" means the time over which the exposure is averaged. For noncarcinogens, the averaging time typically equals the exposure duration. For carcinogens, the averaging time equals the life expectancy of a person.*

The MTCA cleanup level equations for carcinogens include a default averaging time of 75 years. The default value was included in the original cleanup standard provisions adopted in 1991. Ecology's rationale for the use of a 75-year averaging time was summarized in the Responsiveness Summary prepared for the 1991 rule amendments and included two main points:

- *Statistical Data: Statistical data on life expectancy are published yearly by the U.S. Department of Commerce. Data for the year 1985 indicate that life expectancy of the total population is 74.7 years, for males 71.2 years, and for females 78.2 years (Bureau of Census 1986).*
- *Consistency with the Federal Program: The use of a 75 year lifetime is consistent with the approaches recommended by EPA Region X Statement of Work RI/FS/Risk Assessment Deliverables (EPA, 1990b), the Exposure Factors Handbook (EPA 1989b), and the EPA Risk Assessment Guidance for Superfund (EPA, 1989a).* (Washington Department of Ecology, 1991, p. 67)

Since 1991, the average life expectancy has continued to increase in the United States.[1,2] Data for the year 2004 indicate that life expectancy at birth was 77.8 years (75.2 years for males and 80.2 years for females). However, many of the current risk assessment guidance materials recommend the use of a 70-year averaging time for carcinogens (see below).

Draft Definition

Ecology will be considering revisions to MTCA policies and parameters for establishing cleanup standards. The averaging time (AT) is one of the risk parameters used to calculate cleanup levels. Ecology has developed the following definition for review and consideration by the Science Advisory Board and other interested individuals and organizations:

> **"Averaging time"** means the time over which the exposure is averaged. For noncarcinogens, the averaging time typically equals the exposure duration. For carcinogens, the averaging time typically equals 70 years or other values consistent with the assumptions used to develop the cancer slope factor ~~the life expectancy of a person~~.

Rationale for Draft Definition

Ecology considered information on life expectancy and federal guidance when preparing the original definition in 1991. As noted above, the average life expectancy has continued to increase. However, EPA now recommends that risk assessors use an averaging time (70 years) when evaluating cancer risks. The rationale for the draft definition includes the following:

- The revised definition is consistent with current EPA guidance. The EPA Exposure Factors Handbook[3] recommends that risk assessors use exposure parameters that are consistent with the exposure parameters used in the dose-response relationship.

  > *When calculating risk estimates for a specific population, whether the entire national population or some sub-population, the exposure information (either from this handbook or from other data) must be combined with dose-response information. The latter typically comes from the IRIS data base, which summarizes toxicity data for each agent separately. Care must be taken that the assumptions about population parameters in the dose-response analysis are consistent with the population parameters used in the exposure analysis. This Appendix discusses procedures for insuring this consistency.*
  >
  > *In the IRIS derivation of threshold based dose-response relationships (U.S. EPA, 1996), such as the RfD and the RfCs based on adverse systemic effects, there has generally been no explicit use of human exposure factors. In these cases the numerical value of the RfD and RfC comes directly from*

[1] U.S. National Center for Health Statistics. 2007. National Vital Statistics Reports, Vol. 55, No. 19, August 21, 2007.
[2] Managers of the state pension investment fund estimate the Washington's average life expectancy increases by about 2 years every decade. (Wilson, A. 2008. What's the life span of a public employee? The Olympian, May 24, 2008.
[3] U.S. Environmental Protection Agency. 1997. Exposure Factors Handbook. National Center for Environmental Assessment. Washington DC.

animal dosing experiments (and occasionally from human studies) and from the application of uncertainty factors to reflect issues such as the duration of the experiment, the fact that animals are being used to represent humans and the quality of the study. However in developing cancer dose-response (D-R) assessments, a standard exposure scenario is assumed in calculating the slope factor (i.e., human cancer risk per unit dose) on the basis of either animal bioassay data or human data. This standard scenario has traditionally been assumed to be typical of the U.S. population: 1) body weight = 70 kg; 2) air intake rate = 20 m /day; 3) drinking water intake = 2 liters/day; 4) lifetime = 70 years…(EPA, 1997, p. 1 of Appendix 1A)

The draft definition is also consistent with the recommendations in the 2005 Supplemental Guidance for Assessing Susceptibility From Early Life Exposure to Carcinogens, media-specific screening levels developed by EPA Regions 6 and 10 and approaches being used to characterize health risks at individual sites (e.g., Lower Duwamish Waterway Remedial Investigation, appendix B: Baseline Human Health risk Assessment, Final).

- The draft definition is consistent with approaches being used by other state environmental agencies and programs. Many other state environmental agencies use 70 year averaging time to establish risk-based concentrations. For example:
  - The Oregon Department of Environmental Quality (ODEQ) uses a 70 year averaging time to derive risk based concentrations for carcinogens.[4]
  - The California Environmental Protection Agency (Cal-EPA) uses a 70 year averaging time when developing Cancer Potency Factors and health risk assessment based on those values.[5]
  - The Michigan Department of Environmental Quality (MDEQ) uses a 70 year averaging time to calculate risk-based screening concentrations for carcinogens.[6]
- The draft definition is consistent with continued reliance on cancer slope factors published in the IRIS database. Ecology plans to continue to establish cleanup levels using the toxicity information published in the IRIS database. The draft definition is consistent with the procedures and assumptions used to develop cancer slope factors that are published in EPA's database. The draft definition also provides the flexibility to use other averaging times if different assumptions are used to prepare cancer slope factors for individual substances.
- The practical implications of the revised definition will need to be evaluated during the rulemaking process: The use of a 70 year averaging time will result in cleanup levels that are about 7% lower than cleanup levels based on 75 year averaging time (assuming other parameters remain unchanged). Ecology will be evaluating the incremental costs and benefits of the revised definition before making a final decision on rule changes.

---

[4] Web location: http://www.deq.state.or.us/lq/rbdm.htm; under Calculating RBCs for Total Petroleum Hydrocarbons. XLS in the Exposure Factors Worksheet.

[5] Air Toxics Hot Spots Program Risk Assessment Guidelines, Part II Technical Suport Document for Describing Available cancer Potency Factors, May 2005, page B-27

[6] Technical Support document-Attachment 6, April 2005,Part 201 Soil Direct Contact Criteria, Part 213 Tier I Soil Direct Contact Risk-Based Screening Levels, page3// http://www.deq.state.mi.us/documents/deq-rrd-OpMemo_1-Attachment6.pdf)

Definition and Use of Bioaccumulation Factors

Question for Science Advisory Board

Is the draft definition and use of bioaccumulation factor (BAF) values consistent with current scientific information on the bioaccumulation of hazardous substances in aquatic organisms?

Background

The MTCA Cleanup Regulation includes methods and policies for establishing cleanup levels that are based on preventing human health risks resulting from the uptake of hazardous substances into fish and shellfish. For example, the MTCA rule includes the following equation for establishing surface water cleanup levels based on preventing unacceptable non-cancer health risks.

Surface Water Cleanup Standards [Equation 730-1]

$$\text{Surface water cleanup level} = \frac{RfD \times ABW \times UCF1 \times UCF2 \times HQ \times AT}{BCF \times FCR \times FDF \times ED}$$

Where:

RfD =	Reference Dose as specified in WAC 173-340-708(7) (mg/kg-day)
ABW =	Average body weight during the exposure duration (70 kg)
UCF1 =	Unit conversion factor (1,000 ug/mg)
UCF2 =	Unit conversion factor (1,000 grams/liter)
BCF =	Bioconcentration factor as defined in WAC 173-340-708(9) (liters/kilogram)
FCR =	Fish consumption rate (54 grams/day)
FDF =	Fish diet fraction (0.5) (unitless)
HQ =	Hazard quotient (1) (unitless)
AT =	Averaging time (30 years)
ED =	Exposure duration (30 years)

The procedures use bioconcentration factors (BCF) values to estimate the relationship between hazardous substances in surface water and fish and shellfish tissue. The MTCA rule includes the following definition:

> **"Bioconcentration factor"** means the ratio of the concentration of a hazardous substance in the tissue of an aquatic organism divided by the hazardous substance concentration in the ambient water in which the organism resides.

The BCF is a measure of the extent of chemical partitioning between and their surrounding environment. The BCF does not take into account any uptake through the diet, only through contact with environmental media. From a practical standpoint, most available information on

bioconcentration is based on aquatic ecosystems and processes where there is a net accumulation of a chemical directly from water to aquatic organisms resulting from simultaneous uptake (e.g., by gill or epithelial tissue) and elimination. In this sense, bioconcentration represents the first step in the bioaccumulation/biomagnification process.[7]

Most federal and state environmental agencies currently use bioaccumulation factors[8] when characterizing a chemical's bioaccumulation potential. EPA's Office of Water has developed the following definition which reflects the concept that bioaccumulation results from uptake through ingestion as well as contact with the surrounding environmental media:

> **Bioaccumulation factor (BAF).** The ratio (in liters per kilogram of tissue) of the concentration of a chemical in the tissue of an organism to its concentration in water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time. The BAF is calculated as:
>
> $$\mathbf{BAF = C_t/C_w}$$
>
> Where:
>
> C_t = Concentration of the chemical in tissue.
>
> C_w = Concentration of the chemical in water.

Draft Definition

Ecology will be considering revisions to MTCA policies and procedures for hazardous substances that bioaccumulate or biomagnify in the aquatic environment. On step is defining the key parameters used in evaluating this exposure pathway. Ecology has developed the following definition for review and consideration by the Science Advisory Board and other interested individuals and organizations:

> ***"Bioaccumulation factor"*** *or* ***"BAF"*** *means the ratio of the concentration of a hazardous substance in the tissue of an organism to its concentration in the medium of concern (e.g., soil, surface water, or sediment) in situations where both the organism and its food are exposed and the ratio does not change substantially over time. The BAF takes into account both the direct exposure of the organism to the medium of concern and indirect exposure of the organism through ingestion of food sources that are exposed to the medium of concern.*

Rationale for Draft Definition

Ecology considered several factors when preparing the draft definition. The rationale for the draft definition includes the following reasons:

- Ecology believes that the bioaccumulation factor is a more meaningful measure than the bioconcentration factor that is consistent with current scientific information on the bioaccumulation of hazardous substances in aquatic and terrestrial environments. Ecology establishes surface water cleanup levels to prevent unacceptable health risks associated with the bioaccumulation of hazardous substance in fish and shellfish tissues. Cleanup levels based on BCF values only take

[7] Biomagnification occurs when the processes of bioconcentration and bioaccumulation result in increasing tissue concentrations as a chemical moves up the food web (e.g., moves up two or more trophic levels). The term implies an efficient transfer of chemical from food to consumer, so that residue concentrations increase from one trophic level to another.

[8] Regulatory agencies also use "Biota-Sediment Accumulation Factors" or "BSAFs" when establishing sediment cleanup levels. The BSAF is the relative concentration of a substance in the tissues of an organism compared to the concentration of the same substance in the sediment (EPA, 2000). BSAFs are typically developed on a site- or species-specific basis and, consequently, take into account metabolism, growth and bioavailability. Ecology plans to consider the use of BSAF values when evaluating revisions to the sediment cleanup provisions in the Sediment Management Standards (SMS) and MTCA rules.

into account the uptake and retention of hazardous substances by an aquatic organism from water. However, studies have shown that dietary exposure may be more important in determining the ultimate tissue concentrations and health risks (EPA, 2000, EPA, 2002). For some hazardous substances (particularly those that are highly persistent and hydrophobic), the magnitude of bioaccumulation by aquatic organisms can be substantially greater than the magnitude of bioconcentration. For such substances, a cleanup level based on bioconcentration alone may underestimate the extent of bioaccumulation in aquatic media.

Ecology believes that the draft definition is consistent with current scientific information on the bioaccumulation of hazardous substances:

- The draft definition incorporates the concept that multiple routes of exposure (e.g., food, water, sediment) can be important contributors to uptake and retention of hazardous substances in aquatic and terrestrial organisms.
- The draft definition incorporates the concept of steady-state conditions and repeated exposure that are inherent in the bioaccumulation processes and the methods used to characterize those processes.
- The draft definition provides the flexibility to consider the amount of bioaccumulation that occurs at different trophic levels.
- The draft definition provides the flexibility to utilize different methods and procedures to characterize the bioaccumulation potential of a hazardous substance (see below).

- <u>The proposed definition is consistent with definitions used by EPA programs and other Ecology programs</u>: Ecology reviewed definitions used by various EPA programs. For example:
  - **EPA's Office of Water** defines "***bioaccumulation factor (BAF)***" as "...[t]he ratio (in liters per kilogram of tissue) of the concentration of a chemical in the tissue of an aquatic organism to its concentration in water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time. (p 2-1)
  - **EPA's Office of Pollution Prevention and Toxic Substances (OPPTS)** defines "***bioaccumulation factor (BAF)***" as "...the ratio of a substance's concentration in tissue of an aquatic organism to its concentration in the ambient water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time.[9]
  - **The EPA Metals Assessment Framework**[10] defines "***bioaccumulation factor (BAF)"*** as "...the ratio of the chemical concentration in tissue to its concentration in water (using the steady-state method) or as a ratio of uptake rate (ku) and elimination rate (ke) constants (using the kinetic method)…." (p. 5-11)
- <u>Ecology's use of bioaccumulation factors when establishing cleanup standards is consistent with approaches used by EPA programs and other Ecology programs</u>: Most EPA programs emphasize the use of BAFs when estimating the uptake of hazardous substances into fish and shellfish. For example, EPA (2003) includes the following equation for calculating surface water quality criteria based on non-cancer health effects.

[9] 64 FR 703

[10] EPA. 2007. Framework for Metals Risk Assessment. Office of the Science Advisor. Risk Assessment Forum. U.S. Environmental Protection Agency, Washington, DC 20460. EPA 120/R-07/001.

EPA Method for Establishing Surface Water Quality Criteria

Ambient water quality criterion (ug/l) $= \text{RfD} \times \text{RSC} \times \left(\frac{\text{BW}}{\text{DI} + (\sum \text{Fi}_i \times \text{BAF}_i)} \right)$

Where:

RfD	=	Reference Dose (mg/kg-day)
RSC	=	Relative source contribution to account for non-water exposure.
BW	=	Human body weight (kg)
DI	=	Drinking water intake (L/day)
FI_i	=	Fish and shellfish intake (kg/day) at trophic level i (i = 2, 3, 4)
BAF_i	=	Bioaccumulation factor (L/kg) at trophic level i (i = 2, 3, 4)

Several Ecology programs currently use BAF values when estimating the uptake of hazardous substances into fish and shellfish.

- Ecology's Solid Waste and Financial Assistance Program (SWFAP) published a rule for identifying and phasing out Persistent, Bioaccumulative Toxins (PBTs) in 2005. In developing the PBT rule, Ecology recognized that several measures could be used to characterize the bioaccumulation potential (BAF values, BCF values, etc.) of hazardous substances. In general, Ecology used BAF values when such values were available. This is consistent with the approach EPA used to evaluate PBT chemicals.[11]
- Ecology's Water Quality Program and Environmental Assessment Program prepare water quality assessment for rivers, lakes and marine waters in the state. In preparing those assessments, Ecology uses BAFs to evaluate human health impacts. For example, the Environmental Assessment Program used a site-specific BAF to evaluate the health risks posed by elevated levels of DDT in Lake Chelan.[12]

- <u>The draft definition and Ecology's use of bioaccumulation factors takes into account the quality of available information</u>: The draft definition provides the flexibility to use several approaches to estimate bioaccumulation factors. These approaches include:
  - Measured BAFs' derived from data obtained from a field study (i.e., field-measured BAFs)
  - BAFs predicted from biota sediment accumulation factors (BSAFs) obtained from a field study (i.e., field-measured BSAFs)
  - BAFs predicted from laboratory-measured BCF, with or without adjustment by a food chain multiplier
  - BAFs predicted from a chemical's n-octanal-water coefficient (K_{ow}) with or without adjustment by a food chain multiplier.

[11] EPA assigned higher preferences to sources of BAF values than to sources of BCF values when identifying and ranking PBT chemicals.
[12] Ecology. 2006. Lake Chelan DDT and PCBs in Fish Total Maximum Daily Load Study. June 2005 (Revised December 2006). Publication No. 05-03-014.

- There are several readily available sources of information on BAF values in the scientific literature or through various databases. These include: (1) risk profiles prepared for individual chemicals by the World Health Organization, the European Union or the United Nations Environmental Program; (2) information on BAF values compiled by the Oakridge National Laboratory; and (3) bioaccumulation information compiled in the ECOTOX database maintained by the Environmental Protection Agency.
- The practical implications of the revised definition will need to be evaluated during the rulemaking process: The use of a BAF value to establish cleanup levels will generally be more stringent cleanup levels based on BCF values (assuming other parameters remain unchanged). Ecology will be evaluating the incremental costs and benefits of the revised definition before making a final decision on rule changes.

Definition of Carcinogen

Question for Science Advisory Board

Is the draft definition of carcinogen consistent with current scientific information?

Background

The MTCA Cleanup Regulation includes methods and policies for establishing cleanup levels that are based on preventing human health risks. The rule includes separate methods for carcinogens and non-carcinogens. The current rule includes this definition:

> ***"Carcinogen"*** *means any substance or agent that produces or tends to produce cancer in humans. For implementation of this chapter, the term carcinogen applies to substances on the United States Environmental Protection Agency lists of A (known human) and B (probable human) carcinogens, and any substance that causes a significant increased incidence of benign or malignant tumors in a single, well conducted animal bioassay, consistent with the weight of evidence approach specified in the United States Environmental Protection Agency's Guidelines for Carcinogen Risk Assessment as set forth in 51 FR 33992 et seq.*

EPA's Guideline for Carcinogen Risk Assessment (51 FR 33992-34003, September 24, 1986) provided alpha-numeric descriptors of the likelihood that a chemical or other agent is a human carcinogen. These alpha-numeric descriptors were based on a weight-of-evidence approach considering all available information relevant to evaluate the potential for a chemical's carcinogenicity and judging the quality of the available studies. The table below describes weight of evidence categories that describes the likelihood that a chemical or other agent is a human carcinogen:

EPA's Weight of Evidence Classification For Carcinogens in the 1986 Guidelines for Carcinogen Risk Assessment

Weight of Evidence Category	Description
A	Human Carcinogen
B	Probably Human Carcinogen
B-1	Limited human data available
B-2	Sufficient evidence in animals and inadequate or no evidence in humans
C	Possible human carcinogen
D	Not classifiable as to human carcinogenicity
E	Evidence of non-carcinogenicity for humans

US EPA. Workshop Report on EPA Guidelines for Carcinogen Risk Assessment: Use of Human Evidence. U.S. Environmental Protection Agency, Risk Assessment Forum, Washington, DC, EPA/625/3-90/017, 1989.

On March 29, 2005, EPA issued "Guidelines for Carcinogen Risk Assessment"[13] which replaced the 1986 cancer risk guidelines. The 2005 guidelines include a new set of weight of evidence descriptors that replace the previous system (A, B1, B2, C and D). Under the updated EPA guidelines, EPA will prepare a *weight of evidence narrative* (one to two pages) that explains an agent's human carcinogenic potential. EPA's conclusions about human carcinogenic potential are summarized through the use of one or more descriptors that represent points along a continuum of evidence. The EPA descriptors include the following:

- Carcinogenic to Humans
- Likely to Be Carcinogenic to Humans
- Suggestive Evidence of Carcinogenic Potential
- Inadequate Information to Assess Carcinogenic Potential
- Not Likely to Be Carcinogenic to Humans

Additional information on the EPA weight of evidence descriptors are summarized in Table 3 at the end of this section.

Draft Definition

Ecology has reviewed this issue and developed the following definition for review and consideration by the Science Advisory Board and other interested individuals and organizations:

> ***"Carcinogen"*** *means any hazardous substance or group of hazardous substances that is known or suspected to increase the probability of developing cancer. For purposes of implementing this chapter, the term carcinogen applies to substances that have been identified as "carcinogenic to humans" or "likely to be carcinogenic to humans" by the Environmental Protection Agency; as a Group 1, 2A or 2B carcinogen by the International Agency for Research on Cancer; or as a "known to be a human carcinogen" or "reasonably anticipated to be a human carcinogen" by the National Toxicology Program.*

Rationale for Draft Definition

Ecology considered several factors when preparing the draft definition. The rationale for the draft definition includes the following reasons:

- <u>The draft definition incorporates the current EPA cancer risk guidelines</u>. One of Ecology's rulemaking objectives is to maximize consistency with other regulatory agencies. The current MTCA definition is based on the EPA cancer risk guidelines published in 1986. As noted above, EPA issued updated guidelines in March 2007. Ecology believes that the 2005 cancer guidelines represent a sound approach that incorporates scientific information on carcinogenicity that has become available since EPA published the 1986 guidelines.

- <u>The draft definition will promote decisions that are based on current scientific information.</u> One of Ecology's overall rulemaking objectives is to promote decisions that are consistent with current scientific knowledge. The revised definition incorporates determinations on carcinogenicity that are developed by several authoritative scientific bodies (the Environmental Protection Agency, the International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP)). These organizations are generally acknowledged as authoritative scientific bodies on cancer assessment issues. These organizations perform thorough reviews of available scientific information, provide extensive documentation on rationale for determinations on carcinogenicity

[13] Environmental Protection Agency. 2005. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum, Washington DC. EPA/630/P-03/001F. March 2005.

and provide opportunities for extensive scientific peer review. The three agencies use similar carcinogen classification criteria.

Ecology decided to revise the definition to include determinations by the NTP and IARC because of recent findings by the General Accounting Office (GAO). The GAO recently completed a review of EPA's process for performing chemical assessments.[14] They concluded:

> *…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)

- The draft definition will promote decisions that protect human health and the environment. Ecology believes that the draft definition is a health-protective approach that recognizes the uncertainties concluded that the suggested changes would not significantly alter the overall protectiveness of MTCA Cleanup Regulations.
- The draft definition supports the MTCA framework by balancing predictability and flexibility. One of Ecology's overall rulemaking objectives is to provide greater predictability on agency decision-making processes and criteria while at the same time retaining enough flexibility to consider new scientific information. Ecology believes that by identifying clear decision-making criteria and processes, the MTCA rule will promote more timely and consistent decisions.
- The draft definition is consistent with definitions used by other Ecology Programs. One of Ecology's rulemaking objectives is to develop decision-making criteria and processes that are consistent with other Ecology programs. TCP believes that the draft definition is consistent with definitions used by other Ecology programs. For example:
  - **Ecology's Solid Waste and Financial Assistance Program** defines **"Carcinogen"** as **"…**a chemical or chemical group that has been identified as "carcinogenic to humans" or "likely to be carcinogenic to humans" by the Environmental Protection Agency, as a Group 1, 2A or 2B carcinogen by the International Agency for Research on Cancer or as a "known to be a human carcinogen" or "reasonably anticipated to be a human carcinogen" by the National Toxicology Program."
  - **Ecology's Hazardous Waste and Toxic Reduction (HWTR) Program** defines "**Carcinogenic**" as "...a material known to contain a substance which has sufficient or limited evidence as a human or animal carcinogen as listed in both IARC and either IRIS or HEAST."
  - **Ecology's Water Quality Program** defines "**Carcinogen**" as "...any substance or agent that produces or tends to produce cancer in humans. For implementation of this chapter, the term carcinogen will apply to all substances on the United States Environmental Protection Agency Integrated Risk Information System, IRIS data base, of A (known human) and B1 and B2 (probable human) carcinogens for which IRIS listed an oral slope factor."
- The practical implications of the revised definition will need to be evaluated during the rulemaking process: Ecology does not believe that the draft definition will result in a significant changer (either up or down) in the number of substances identified as carcinogens. However, Ecology will evaluate the incremental costs and benefits of the revised definition before making a final decision on rule changes.

[14] 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.

Weight of Evidence Descriptors Used by the Environmental Protection Agency to Characterize Carcinogenic Hazard Potential		
Descriptor	**Summary**	**Examples**
Carcinogenic to Humans	Strong evidence of human carcinogenicity. It covers different combinations of evidence.	• Convincing epidemiologic evidence of a causal association between human exposure and cancer. • Lesser weight of epidemiologic evidence that is strengthened by other lines of evidence.
Likely to Be Carcinogenic to Humans	Weight of the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor "Carcinogenic to Humans."	• An agent demonstrating a plausible (but not definitively causal) association between human exposure and cancer, mostly with some supporting biological, experimental evidence, though not necessarily carcinogenicity data from animal experiments; • An agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans; • A positive tumor study that raises additional biological concerns beyond that of a statistically significant result, for example, a high degree of malignancy, or an early age at onset; • A rare animal tumor response in a single experiment that is assumed to be relevant to humans; or • A positive tumor study that is strengthened by other lines of evidence.
Suggestive Evidence of Carcinogenic Potential	Weight of evidence is suggestive of carcinogenicity; a concern for potential carcinogenic effects in humans is raised, but the data are judged not sufficient for a stronger conclusion.	• A small, and possibly not statistically significant, increase in tumor incidence observed in a single animal or human study that does not reach the weight of evidence for the descriptor "Likely to Be Carcinogenic to Humans." • A small increase in a tumor with a high background rate in that sex and strain, when there is some but insufficient evidence that the observed tumors may be due to intrinsic factors that cause background tumors and not due to the agent being assessed. • Evidence of a positive response in a study whose power, design, or conduct limits the ability to draw a confident conclusion (but does not make the study fatally flawed), but where the carcinogenic potential is strengthened by other

		lines of evidence; or • Statistically significant increase at one dose only, but no significant response at the other doses and no overall trend.
Inadequate Information to Assess Carcinogenic Potential	Available data are judged inadequate for applying one of the other descriptors.	• Little or no pertinent information; • Conflicting evidence, that is, some studies provide evidence of carcinogenicity but other studies of equal quality in the same sex and strain are negative. Positive results in some studies and negative results in one or more different experimental systems do not constitute conflicting evidence; or • Negative results that are not sufficiently robust for the descriptor, "Not Likely to Be Carcinogenic to Humans."
Not Likely to Be Carcinogenic to Humans	Available data are considered robust for deciding that there is no basis for human hazard concern.	• Animal evidence that demonstrates lack of carcinogenic effect in both sexes in well-designed and well-conducted studies in at least two appropriate animal species, • Convincing and extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans, • Convincing evidence that carcinogenic effects are not likely by a particular exposure route, or • Convincing evidence that carcinogenic effects are not likely below a defined dose range.

Carcinogen Classification Criteria Used By the International Agency for Research on Cancer (IARC)		
Group 1	The agent is carcinogenic to humans. This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.	***Sufficient evidence of carcinogenicity in humans***: The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. ***Limited evidence of carcinogenicity in humans***: A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
Group 2A	The agent is probably carcinogenic to humans. This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited evidence of carcinogenicity* in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.	***Sufficient evidence of carcinogenicity in animals***: The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in: • Two or more species of animals or • Two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. • An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*. • A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumor or age at onset, or when there are strong findings of tumors at multiple sites. ***Limited evidence of carcinogenicity in humans (SEE ABOVE).*** ***Inadequate evidence of carcinogenicity in humans***: The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.
Group 2B	The agent is possibly carcinogenic to humans. This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than	***Limited evidence of carcinogenicity in humans (SEE ABOVE).*** ***Sufficient evidence of carcinogenicity in animals (SEE ABOVE)***

	sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.	***Inadequate evidence of carcinogenicity in humans (SEE ABOVE)***
Group 3	The agent is not classifiable as to its carcinogenicity to humans. This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals. Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents that do not fall into any other group are also placed in this category. An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.	
Group 4	The agent is probably not carcinogenic to humans. This category is used for agents for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents for which there is *inadequate evidence of carcinogenicity* in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group.	

Evaluation Criteria Used by the National Toxicology Program to Identify Carcinogens (NTP, 2005)	
Known To Be Human Carcinogen:	There is sufficient evidence of carcinogenicity from studies in humans*, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer. *This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question that can be useful for evaluating whether a relevant cancer mechanism is operating in people.
Reasonably Anticipated To Be Human Carcinogen:	There is limited evidence of carcinogenicity from studies in humans*, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded; or there is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset; or there is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.