RISK CHARACTERIZATION

OVERVIEW: Risk characterization (also referred to in the CTSA process as risk integration) is the integration of hazard and exposure information to quantitatively or qualitatively assess risk. Risk characterization typically includes a description of the assumptions, scientific judgments, and uncertainties that are part of this process.

The level of risk characterization necessary in a CTSA varies depending on the differences between the substitutes being assessed in the use cluster. The risk characterization identifies, in a manner that facilitates decision-making, the areas of concern as they differ among the substitutes. Risks may vary in terms of magnitude, type, or domain of application. If the differences in risk among the substitutes are great, then a detailed, quantitative characterization of risk may not be necessary. If the differences in risk associated with the substitutes are more subtle, then a quantitative analysis may be necessary. The methods outlined here describe a more detailed, quantitative risk characterization.

GOALS:

- Integrate chemical hazard and exposure information to assess and compare risks from ambient environment, consumer, and occupational exposures.
- Provide risk estimates to the Risk, Competitiveness & Conservation Data Summary module.
- Present risk information and discuss uncertainty in a manner that assists in decision-making.

PEOPLE SKILLS: The following lists the types of skills or knowledge that are needed to complete this module.

- Knowledge of risk assessment guidance and methodology.
- Understanding of chemical exposures.
- Understanding of human, other mammalian, and aquatic toxicology.
- Ability to present and interpret the results of risk characterization for decision-making.

Within a business or a DfE project team, the people who might supply these skills include a risk assessment specialist.

Note: The analysis presented in this module should not be undertaken without the assistance of someone with expertise in human health and environmental risk assessment. Furthermore, peer-review of the completed risk characterization is recommended.

DEFINITION OF TERMS: Several terms from the Human Health Hazards Summary, Environmental Hazards Summary, and Exposure Assessment modules are used in the Risk Characterization module and are defined here as well.

Human Health Hazards Summary

Developmental Toxicity: Adverse effects produced prior to conception, during pregnancy, or during childhood. Exposure to agents affecting development can result in any one or more of the following manifestations of developmental toxicity: death, structural abnormality, growth alteration, and/or functional deficit. These manifestations encompass a wide array of adverse developmental end points, such as spontaneous abortion, stillbirths, malformations, early postnatal mortality, reduced birth weight, mental retardation, sensory loss and other adverse functional or physical changes that are manifested postnatally.

International Agency for Research on Cancer (IARC) Classification: A method for evaluating the strength of evidence supporting a potential human carcinogenicity judgment based on human data, animal data, and other supporting data. A summary of the IARC carcinogenicity classification system includes:

- Group 1: Carcinogenic to humans.
- Group 2A: Probably carcinogenic to humans.
- Group 2B: Possibly carcinogenic to humans.
- Group 3: Not classifiable as to human carcinogenicity.
- Group 4: Probably not carcinogenic to humans.

Lowest-Observed Adverse Effect Level (LOAEL): The lowest dose level in a toxicity test at which there are statistically or biologically significant increases in frequency or severity of adverse effects in the exposed population over its appropriate control group.

No-Observed Adverse Effect Level (NOAEL): The highest dose level in a toxicity test at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects in the exposed population over its appropriate control; some effects may be produced at this level, but they are not considered adverse, nor precursors to adverse effects.

Pharmacokinetics: The dynamic behavior of chemicals within biological systems. Pharmacokinetic processes include uptake, distribution, metabolism, and excretion of chemicals.

Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime. RfCs are generally reported as a concentration in air (mg/m^3).

Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime. RfDs are reported as mg/kg-day.

Risk: In general, risk pertains to the probability and severity of adverse effects (e.g., injury, disease, or death) under specific circumstances. In the context of a CTSA, risk is an expression of the likelihood of adverse health or environmental effects from a specific level of exposure; only cancer risk is estimated as a probability. (Also see Cancer Risk, Individual Risk and Population Risk.)

Slope Factor (q_1*): A measure of an individual's excess risk or increased likelihood of developing cancer if exposed to a chemical. It is determined from the upperbound of the slope of the dose-response curve in the low-dose region of the curve. More specifically, q_1* is an approximation of the upper bound of the slope when using the linearized multistage procedure at low doses. The units of the slope factor are usually expressed as 1/(mg/kg-day) or $(mg/kg\text{-}day)^{-1}$.

Unit Risk: The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water or 1 $\mu g/m^3$ in air (with units of risk per $\mu g/m^3$ air or risk per µg/L water).

Weight-of-Evidence Classification (EPA): In assessing the carcinogenic potential of a chemical, EPA classifies the chemical into one of the following groups, according to the weight-of-evidence from epidemiologic and animal studies:

- Group A: Human Carcinogen (sufficient evidence of carcinogenicity in humans).
- Group B: Probable Human Carcinogen (B1 - limited evidence of carcinogenicity in humans; B2 - sufficient evidence of carcinogenicity in animals with inadequate or lack of evidence in humans).
- Group C: Possible Human Carcinogen (limited evidence of carcinogenicity in animals and inadequate or lack of human data).
- Group D: Not Classifiable as to Human Carcinogenicity (inadequate or no evidence).
- Group E: Evidence of Noncarcinogenicity for Humans (no evidence of carcinogenicity in adequate studies).

(The "Proposed Guidelines for Carcinogen Risk Assessment" [EPA, 1996b] propose use of weight-of-evidence descriptors, such as "Likely" or "Known," "Cannot be determined," and "Not likely," in combination with a hazard narrative, to characterize a chemical's human carcinogenic potential - rather than the classification system described above.)

Environmental Hazards Summary

Aquatic Toxicity Concern Concentration (CC): The concentration of a chemical in the aquatic environment below which no significant risk to aquatic organisms is expected.

Exposure Assessment

Acute Potential Dose Rate (APDR): The dose, usually expressed on a per day basis, averaged over a period of time corresponding to an acute exposure period.

Exposure Concentration, Exposure Point Concentration: The chemical concentration, in its transport or carrier medium, at the location of contact with an organism. Also defined, typically for ecological risk, as the *Expected Environmental Concentration* (EEC), or *Predicted Environmental Concentration* (PEC).

Exposure Level: In general, a measure of the magnitude of exposure, or the amount of an agent available at the exchange boundaries (i.e., lungs, gastrointestinal tract, or skin), during some specified time. In the Exposure Assessment and Risk Characterization modules, "exposure level" is used specifically as a measure of exposure expressed as a concentration rather than as a potential dose rate.

Exposure Pathway: The physical course a chemical takes from the source to the organism exposed. An example of an exposure pathway might be inhalation by a worker of volatile organic compounds (VOCs) that have evaporated from a solvent to the air.

Exposure Scenario: A description of the specific circumstances under which exposure might occur, consisting of facts, assumptions, and inferences about how exposure takes place. An exposure scenario may comprise one or more exposure pathways.

Lifetime Average Daily Concentration (LADC): The estimated daily concentration (usually in air) during the exposure duration, averaged over a lifetime.

Lifetime Average Daily Dose (LADD): The estimated potential daily dose rate received during the exposure duration, averaged over a lifetime. LADD is typically expressed in units of mg/kg-day.

Peak Exposure Level or Dose: The maximum exposure level or maximum potential dose rate.

Potential Dose Rate (PDR): The amount of a chemical ingested, inhaled, or applied to the skin per unit time (e.g., in units of mg/day). PDR may also be expressed per unit body weight per unit time (e.g., in mg/kg-day). PDR is the amount of a chemical that is available at the body's exchange boundaries and potentially could be absorbed into the body. (Related terms used elsewhere include "intake" or simply "dose," although the term dose implies that absorption is taken into account while PDR does not. The concepts of intake, dose, and potential dose are described in detail in "Guidelines for Exposure Assessment" [EPA, 1992a].)

Receptor: The organism of interest (human or non-human) involved in a particular exposure pathway.

Risk Characterization

Cancer Risk: The probability of developing cancer over a lifetime as a result of exposure to a potential carcinogen. Cancer risk could be estimated for an individual or a population (see Individual Risk and Population Risk). The cancer risk estimated in a CTSA is the upper bound excess lifetime cancer risk.

Ecological Risk Indicator: The ratio of the exposure concentration (EEC or PEC) to the CC. In ecological risk characterization this approach is typically referred to as the ecological quotient method.

Hazard Index (HI): The sum of more than one hazard quotient for multiple chemicals and/or multiple exposure pathways. Calculation of HI assumes additivity of the chemical effects. This is valid only where the chemicals elicit the same effect by the same exposure route and mechanism of action.

Hazard Quotient (HQ): The ratio of potential rate (PDR) or exposure level for a single chemical over a specified time period to the RfD or RfC for that chemical derived from a similar exposure period.

Individual Risk: An estimate of the probability of an exposed individual experiencing an adverse effect, such as "1 in 1,000" (or 10^{-3}) risk of cancer.

Margin of Exposure (MOE): The ratio of the NOAEL or LOAEL to a PDR or exposure level.

Population Risk: An aggregate measure of the projected frequency of effects among all exposed people, such as "four cancer cases per year."

APPROACH/METHODOLOGY: The following presents a summary of the approach or methodology for conducting a risk characterization. Further details for Steps 1 through 9 are presented in the next section of this module. This summary is intended as an overview of the process, and may vary on a case-by-case basis. The reader is referred to guidance documents (see Table 6-11 for further information).

Step 1: Collect and organize information from the Exposure Assessment, Human Health Hazards Summary, and Environmental Hazards Summary modules.

Human Health Risk (occupational, consumer, etc.)

Step 2: For each chemical in a pathway, calculate the indicator of cancer risk and/or noncancer risk.

- For each chemical that is classified in the hazard summary as a carcinogen, estimate cancer risk.

- For each chemical that exhibits noncancer health effects and for which an RfD or RfC is available (note: this may include chemicals that are also classified as carcinogens), calculate the indicator of noncancer risk, expressed as an HQ.
- For chemicals without a RfD or RfC, calculate the indicator of noncancer risk, expressed as a MOE.

Step 3: For multiple chemicals (e.g., exposure to a formulation made up of a mixture of chemicals), calculate total cancer risk and the noncancer HI for each pathway, using the information from Step 2.

Step 4: If applicable, and exposure is possible via more than one pathway, combine risks across pathways that affect the same individual(s) over the same time periods by summing cancer risks and summing HQs or HIs.

Step 5: If applicable, calculate population cancer risk.

Step 6: Discuss and assess sources of uncertainty and variability of risk characterization results.

Step 7: Summarize and present the risk characterization results. The chemical- and pathway-specific results from Step 2 as well as totals from Steps 3 and 4 (if applicable) and population cancer risk from Step 5 (if applicable) should all be presented. (Large tables of data may be more appropriately included as an appendix to the Risk Characterization module.)

Environmental (aquatic) Receptors

Step 8: Compare CC for each chemical to the exposure concentration (EEC or PEC). Typically, this is done for the aquatic environment. A numerical indicator of ecological risk may also be calculated as the ratio of the exposure concentration to the CC. This approach is typically referred to as the ecological quotient method.

Transfer Information

Step 9: Provide human health and environmental risk information to the Risk, Competitiveness & Conservation Data Summary module. Express risk characterization information on a "per unit of production" basis, if applicable.

METHODOLOGY DETAILS: This section presents methodology details for completing Steps 1 through 9. Additional information on these and other steps can be found in the published guidance (see Table 6-11: Published Guidance on Risk Characterization). In addition, an example of background information on risk assessment is presented in Appendix D, from the Screen Reclamation CTSA (EPA, 1994c).

Details: Step 1, Collecting and Organizing Data

Data to be provided by the Human Health Hazards Summary module include:

- Characterization of chemicals by hazard type: carcinogenicity, acute or chronic toxicity, developmental toxicity, etc.
- q_1* or unit risk, and weight-of-evidence for chemicals classified as carcinogens.
- RfD and/or RfC for chemicals that exhibit noncancer toxicity.
- LOAEL or NOAEL for chemicals where an RfD or RfC is not available.
- Pharmacokinetic data (e.g., chemical absorption factors).

Data to be provided by the Environmental Hazards Summary module include the CC.

Data to be provided by the Exposure Assessment module include:

- Outline of exposure scenarios, population(s) of interest, and pathways to be evaluated (these are described in the Exposure Assessment module).
- Potential dose rates (e.g., the PDR, LADD, and APDR).
- Exposure levels (e.g., the lifetime average exposure level, and the peak exposure level [expressed as concentrations]).
- Modeled or measured ambient environmental (water) concentrations.

Details: Step 2, Calculating Chemical Risk

Cancer Risk

For chemicals classified as carcinogens, upper bound excess lifetime cancer risk, expressed as a unitless probability, is typically estimated by the linear low-dose cancer risk equation, where:

$$\text{cancer risk} = \text{LADD} \times q_1^*$$

For example:

for an LADD of 0.3 mg/kg-day and a q_1* of 0.02 $(\text{mg/kg-day})^{-1}$:

$$\text{cancer risk} = (0.3) \times (0.02)$$
$$= 0.006$$

This cancer risk (on an individual basis) would mean a 6 in 1,000 risk of developing cancer from exposure to this particular chemical, in addition to baseline cancer risk.

Alternatively, cancer risk can be calculated by the lifetime average exposure level (in air or water) x unit risk factor (this is a variant of the linear low-dose equation).

For example:

for a lifetime average exposure level of 0.4 $\mu g/m^3$ and a unit risk of 0.0002 $(\mu g/m^3)^{-1}$:

$$\text{cancer risk} = (0.4) \times (0.0002)$$
$$= 0.00008 \text{ (or } 8 \times 10^{-5})$$

For higher doses (cancer risks above approximately 0.01), this linear equation is not considered valid. In this case the results should state "risks are above 0.01 but cannot be estimated more exactly." Cancer risk numbers are typically presented to one significant figure.

Noncancer Risk

For chemicals that exhibit noncancer toxicity, an HQ is calculated by:

$$HQ = PDR / RfD$$

For example:

for a PDR of 0.4 mg/kg-day and an RfD of 0.05 mg/kg-day:

$HQ = (0.4) / (0.05)$

$= 8$

Chemicals that exhibit developmental toxicity are evaluated separately, using an RfD for developmental effects (RfD_{DT}). Short-term exposure can be of concern for developmental effects (because of the window of fetal vulnerability) so a peak exposure is used rather than a PDR for the entire duration of exposure:

$$HQ_{DT} = \text{peak exposure} / RfD_{DT}$$

Alternatively, if an RfC (typically for air) or RfC for developmental effects (RfC_{DT}) and corresponding exposure level is available, the HQ can be calculated by:

$$HQ = \text{lifetime average exposure level} / RfC$$

or:

$$HQ_{DT} = \text{peak exposure level} / RfC_{DT}$$

HQs (non-developmental) are typically calculated for long-term (chronic) exposure periods. They can also be calculated for subchronic or acute (shorter-term) exposure periods if subchronic or acute RfD (or RfC) and dose rates (or exposure levels) are determined in the Human Health Hazards Summary and Exposure Assessment modules. It is important to keep the exposure durations consistent; for example, subchronic RfDs combined with subchronic dose rates.

The HQ is based on the assumption that there is a level of exposure (i.e., the RfD) below which it is unlikely, even for sensitive subgroups, to experience adverse health effects. Unlike cancer risk, the HQ does not express *probability* (only the ratio of the estimated dose to the RfD or RfC) and it is not linear; i.e., an HQ of 10 does not mean that adverse health effects are 10 times more likely to occur than for an HQ of 1.

For chemicals where an RfD or RfC is not available, MOE is calculated by:

$$MOE = NOAEL / PDR \text{ or } LOAEL / PDR$$

Alternatively, MOE can be calculated with an exposure level rather than a dose rate:

MOE = NOAEL or LOAEL / lifetime average exposure level

As with the HQ, the MOE is not a probabilistic statement of risk. Very high MOE values, such as values greater than 100 for a NOAEL-based MOE or 1,000 for a LOAEL-based MOE, imply a very low level of concern. As the MOE decreases, the level of concern increases.

Details: Step 3, Calculating Pathway Risk for Multiple Chemicals

For pathways where exposure to more than one chemical is being assessed, the cancer risk results for each chemical are typically summed for each pathway:

$$\text{cancer risk}_{TOT} = \Sigma \text{ cancer risk for each chemical}$$

It should be noted that summing cancer risks assumes additivity of the chemical effects. Risks from exposures to more than one carcinogen are typically assumed to be additive, unless available information suggests otherwise.

The HQs can also be summed to calculate an HI:

$$HI = \Sigma \text{ HQ for each chemical}$$

Alternatively, HI can be calculated by:

$$HI = PDR_1/RfD_1 + PDR_2/RfD_2 + ... + PDR_i/RfD_i$$

Calculation of an HI also assumes additivity of the chemical effects. This is valid only where the chemicals elicit the same effect by the same mechanism of action. Typically, if an HI exceeds unity, the chemicals are segregated by effect and mechanism and segregated HIs recalculated. This segregation by mechanism of action and type of effect is not a simple exercise and should only be performed by an experienced toxicologist.

Details: Step 4, Summing Pathway Risks, if Applicable

In some situations, a receptor may be exposed to a chemical, or a mixture of chemicals, through more than one pathway (for example, a worker may be inhaling volatile chemicals from a solution and at the same time be exposed through the skin). In this case the total risk is equal to the risks from all relevant pathways. Cancer risks can be summed across pathways, where:

$$\text{total exposure cancer risk} = \text{cancer risk (pathway}_1\text{)} + \text{cancer risk (pathway}_2\text{)} + ... \text{ cancer risk (pathway}_i\text{)}$$

HI should be summed separately for different exposure durations (e.g., chronic, subchronic, shorter term durations); an HI for multiple pathways and similar exposure durations can be calculated by:

$$\text{total exposure HI} = \text{HI}(\text{pathway}_1) + \text{HI}(\text{pathway}_2) + \ldots \text{HI}(\text{pathway}_i)$$

Results are typically presented for each pathway separately (Step 3) as well as combined across pathways.

Details: Step 5, Calculating Population Cancer Risk, if Applicable

Cancer risks may be characterized in terms of individual or population risk. Risk to a population is typically calculated by:

cancer risk = individual cancer risk x number in exposed population

Population risks may also be calculated separately for areas with different levels of exposure. Population data sources may include the number in the exposed population from the Exposure Assessment module, census data, or other demographic data or work place surveys.

Details: Step 6, Assessing Uncertainty and Variability

Because information for risk characterization comes from the Environmental Hazards Summary, Human Health Hazards Summary, and Exposure Assessment modules, an assessment of uncertainty should include those uncertainties in the hazard and exposure data. There is also the issue of compounded uncertainty; as uncertain data are combined in the assessment, uncertainties may be magnified in the process. EPA guidance (e.g., *Risk Assessment Guidance for Superfund* [EPA, 1989a]; "Guidelines for Exposure Assessment" [EPA, 1992a]) contains detailed descriptions of uncertainty assessment, and the reader is referred to these for further information.

Uncertainties in the hazard data could include:

- Uncertainties from use of quantitative structure-activity relationships (QSARs) for aquatic toxicity.
- Using dose-response data from high dose studies to predict effects that may occur at low levels.
- Using data from short-term studies to predict the effects of long-term exposures.
- Using dose-response data from laboratory animals to predict effects in humans.
- Using data from homogeneous populations of laboratory animals or healthy human populations to predict the effects on the general human population, with a wide range of sensitivities.
- Assuming 100 percent absorption of a dose when the actual absorption rate may be significantly lower.
- Using toxicological potency factors from studies with a different route of exposure than the one under evaluation.

- Effects of chemical mixtures (effects may be independent, additive, synergistic or antagonistic).
- Possible effects of substances not included because of a lack of toxicity data.
- Carcinogen weight-of-evidence classifications; for any chemicals assessed as carcinogens (described in the Human Health Hazards Summary module), the weight-of-evidence classification should be presented with any cancer risk results.

Uncertainties in the exposure data could include:

- Description of exposure setting - how well the typical facility used in the exposure assessment represents the facilities included in the CTSA; the likelihood of the exposure pathways actually occurring.
- Possible effect of any chemicals that may not have been included because they are minor or proprietary ingredients in a formulation.
- Chemical fate and transport model applicability and assumptions - how well the models and assumptions that are required for fate and transport modeling represent the situation being assessed and the extent to which the models have been verified or validated.
- Parameter value uncertainty, including measurement error, sampling error, parameter variability, and professional judgment.
- Uncertainty in combining pathways for an individual.

In the CTSA, uncertainty is typically addressed qualitatively. Variability in the exposure assessment is typically addressed through the use of "exposure descriptors," which are discussed in the Exposure Assessment module.

Details: Step 7, Summarizing and Presenting Results

The risk characterization results are typically presented in tables, with the cancer risk, HQ and/or HI, and MOE calculated for each chemical. The results are also explained and summarized in the text along with the tables. The actual format of the tables can vary greatly, depending on the complexity of the analysis (the number of chemicals, scenarios, and pathways being assessed). A typical format is shown in Table 6-10.

TABLE 6-10: TYPICAL FORMAT FOR RISK CHARACTERIZATION RESULTS

(e.g., Dermal Contact with Solution X in Occupational Setting Performing Task Y)

Chemical	**Cancer Risk [weight-of-evidence classification]**	**HQ**	**MOE**
chemical *a*	result for *a* [B2]	result for *a*	result for *a*
.	.	.	.
.	.	.	.
.	.	.	.
chemical *z*	result for *z* [B1]	result for *z*	result for *z*
sum of cancer risk, or HI, for pathway:	sum of cancer risks	sum of HQs (when appropriate)	(not summed)

Details: Step 8, Comparing CC to Aquatic Concentrations

Exposure concentrations below the CC are assumed to present low risk to aquatic species. Exposures that exceed the Cc indicate a potential for adverse impact on aquatic species. The level of concern increases as the ratio of exposure concentration to CC increases.

An ecological risk indicator may be calculated as a unitless ratio, for example:

> With a daily stream concentration of 2 mg/l and a CC of 1 mg/l, the ecological risk indicator = (2) / (1) = 2

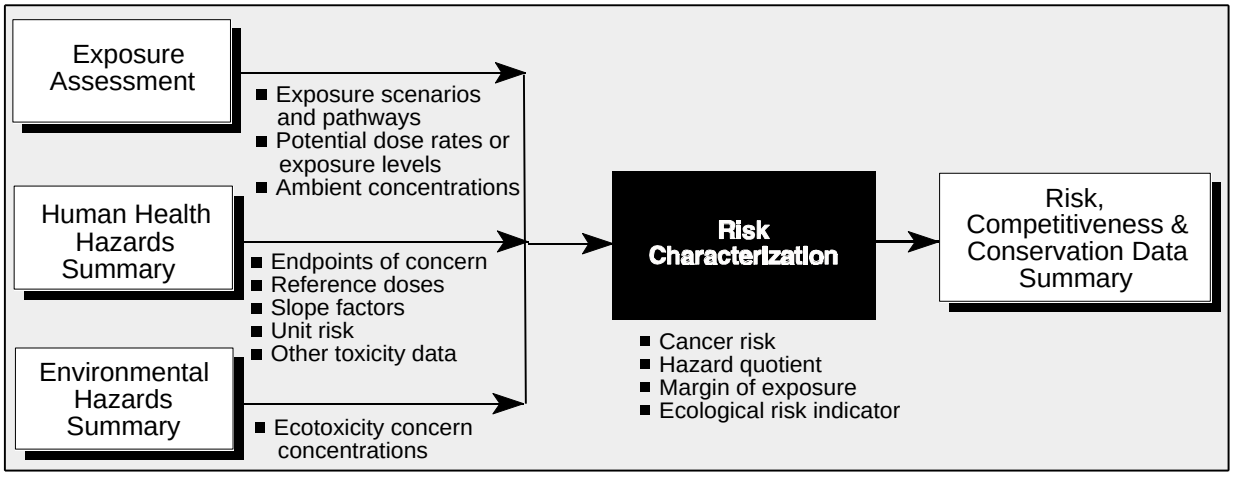
An ecological risk indicator greater than 1 indicates that the estimated or measured chemical concentration exceeds the concentration of concern for the aquatic environment based on chemical toxicity to aquatic organisms. The greater the number of days the CC is exceeded, the greater the potential risk.

Details: Step 9, Expressing Risk on a "Per Unit of Production" Basis

Where possible, also express risk characterization results on a "per unit of production" basis using an amount that is produced during the corresponding exposure period. For example, cancer risk can be expressed as risk/amount produced. This information will facilitate evaluating tradeoffs among alternatives in the Social Benefits/Costs Assessment and Risk, Competitiveness & Conservation Data Summary modules.

FLOW OF INFORMATION: The Risk Characterization module receives information from the Exposure Assessment, Human Health Hazards Summary, and Environmental Hazards Summary modules and transfers information to the Risk, Competitiveness & Conservation Data Summary module. Examples of information flows are shown in Figure 6-5.

FIGURE 6-5: RISK CHARACTERIZATION MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: Table 6-11 presents references for published guidance on risk characterization.

TABLE 6-11: PUBLISHED GUIDANCE ON RISK CHARACTERIZATION

Reference	Type of Guidance
Barnes, D.G. and M. Dourson. 1988. "Reference Dose (RfD): Description and Uses in Health Risk Assessments."	EPA's principal approach to assessing risk for health effects, other than cancer and gene mutations, from chronic chemical exposure.
Habicht, F.H. II. 1992. *Guidance on Risk Characterization for Risk Managers and Risk Assessors.*	Guidance for managers and assessors on describing risk assessment results in EPA reports, presentations, and decision packages with respect to reliability and uncertainty of the results of risk characterization.
Nabholz, J.V. 1991. "Environmental Hazard and Risk Assessment Under the United States Toxic Substances Control Act."	Discussion of environmental risk assessment procedures (as practiced under TSCA).
Nabholz, J.V., et. al. 1993a. "Environmental Risk Assessment of New Chemicals Under the Toxic Substances Control Act (TSCA) Section Five."	Discussion of environmental risk assessment procedures (as practiced under TSCA).
U.S. Environmental Protection Agency. 1987b. *The Risk Assessment Guidelines of 1986*.	Guidance on risk assessment methods; includes *Guidelines for Mutagenicity Risk Assessment, Guidelines for Carcinogen Risk Assessment*, and *Guidelines for the Health Risk Assessment of Chemical Mixtures*, originally published in the September 24, 1986 *Federal Register*, FR 51(185).
U.S. Environmental Protection Agency. 1989a. *Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A).*	Detailed guidance for developing health risk information at Superfund sites; may also be applicable to other assessments of hazardous wastes and hazardous materials.
U.S. Environmental Protection Agency. 1990a. *Exposure Factors Handbook.*	Data related to exposure frequency and duration, and other human physiological and activity parameters.
U.S. Environmental Protection Agency. 1991b. "Guidelines for Developmental Toxicity Risk Assessment."	Guidance on assessing developmental toxicity risks; a revision of the *Guidelines for the Health Risk Assessment of Suspect Developmental Toxicants*, FR 51(185), September 24, 1986.

TABLE 6-11: PUBLISHED GUIDANCE ON RISK CHARACTERIZATION	
Reference	**Type of Guidance**
U.S. Environmental Protection Agency. 1991f. *Human Health Evaluation Manual, Supplemental Guidance:* "Standard Default Exposure Factors."	Exposure factors guidance to be used in the Superfund remedial investigation/feasibility study process.
U.S. Environmental Protection Agency. 1992a. "Guidelines for Exposure Assessment."	EPA guidance on exposure assessment; assessing uncertainty and variability in exposure data.
U.S. Environmental Protection Agency. 1994i. *Guidelines for Reproductive Toxicity Assessment.*	Guidance on assessing reproductive toxicity risks.
U.S. Environmental Protection Agency. 1994j. *Pesticide Occupational and Residential Cancer Risk Policy Statement.*	EPA's risk management policy with regard to occupational and residential (not dietary) cancer risks resulting from the use of pesticides. (Reflects Assistant Administrator's policy direction on risk which may be applicable to OPPT programs.)
U.S. Environmental Protection Agency. 1994k. "Final Report: Principles of Neurotoxicity Risk Assessment."	Guidance on assessing neurotoxic risks.
U.S. Environmental Protection Agency. 1994l. *OPPT Risk Assessment SOPs.*	A collection of guidance documents on various EPA exposure and risk characterization procedures.
U.S. Environmental Protection Agency. 1996b. "Proposed Guidelines for Carcinogen Risk Assessment."	Guidance on assessing carcinogenic risks; a revision of the *Guidelines for Carcinogen Risk Assessment*, FR 51(185), September 24, 1986.
Zeeman, M.G. 1995a. "EPA's Framework for Ecological Effects Assessment."	Provides an overview of the process used in the environmental toxicity assessment of chemicals
Zeeman, M.G. 1995b. "Ecotoxicity Testing and Estimation Methods Developed under Section 5 of the Toxic Substances Control Act (TSCA)."	Describes the developoment, validation, and application of SARs in the EPA OPPT.

Note: References are listed in shortened format, with complete references given in the reference list following Chapter 10.

DATA SOURCES: Hazard and exposure data are provided by the Human Health Hazards Summary, Environmental Hazards Summary, and Exposure Assessment modules.