Chapter 5

CHEMICAL & PROCESS INFORMATION

This chapter presents module descriptions for the chemical and process information component of a CTSA which consists of nine data gathering modules:

- Chemical Properties.
- Chemical Manufacturing Process & Product Formulation.
- Environmental Fate Summary.
- Human Health Hazards Summary.
- Environmental Hazards Summary.
- Chemistry of Use & Process Description.
- Process Safety Assessment.
- Market Information.
- International Information.

The Chemical Properties, Environmental Fate Summary, Human Health Hazards Summary, and Environmental Hazards Summary modules collect data on the properties of the chemicals in the use cluster. The Chemical Manufacturing Process & Product Formulation, Chemistry of Use & Process Description, Process Safety Assessment, Market Information, and International Information modules collect data relating to the chemicals themselves, and/or the substitute products, processes, or technologies in which they are used. The information compiled in each of these modules is used later in the data analysis components of a CTSA.

For example, the Chemical Properties module provides chemical identity information to almost every module in the CTSA. Among other things, this minimizes the potential for confusion caused by chemical synonyms and ensures that DfE team members from different disciplines have a common point of reference on chemical names. The Hazards Summary modules combine with data from the Exposure Assessment module to characterize human health and ecological (aquatic) risks. The Chemistry of Use & Process Description module clearly defines the processes in the use cluster so that DfE team members working on different process-related modules have a common understanding of the processes.

Only the Process Safety Assessment, Market Information, and International Information modules of this component provide information directly to the final trade-off evaluations of a CTSA. The Process Safety Assessment module provides data on potential chemical hazards (e.g., fire, explosion, etc.) and precautions for safe use of equipment or chemicals to the Risk, Competitiveness & Conservation Data Summary module for evaluation in the Social Benefits/Costs Assessment and Decision Information Summary modules. The Market Information and International Information modules provide data on domestic and foreign supply and demand and relevant trade issues.

CHEMICAL PROPERTIES

OVERVIEW: Chemical properties, physical properties, and the chemical structure of a substance are characteristics which identify it from other substances. In this module, the physical and chemical characteristics of the chemicals in the use cluster are detailed.

GOALS:

- Identify the physical and chemical characteristics along with the chemical structures of the chemicals in the use cluster.
- Determine a discrete appropriate name and Chemical Abstracts Service Registry Number (CAS RN), defined below for each chemical to be used throughout the assessment.
- Facilitate the identification of potential chemical substitutes with similar properties to the chemicals in the use cluster.
- Provide chemical names and/or properties to the following modules: Chemical Manufacturing Process & Product Formulation, Environmental Fate Summary, Human Health Hazards Summary, Environmental Hazards Summary, Chemistry of Use & Process Description, Process Safety Assessment, Market Information, Workplace Practices & Source Release Assessment, Exposure Assessment, Regulatory Status, Performance Assessment, and Control Technologies Assessment.

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

- Knowledge of the basic concepts of chemistry, particularly physical and chemical properties.

Within a business or DFE project team, the people who might supply these skills include a chemist, chemical engineer, or an environmental scientist.

DEFINITION OF TERMS:

Boiling Point (bp): The temperature at which a liquid under standard atmospheric pressure (or other specified pressure) changes from the liquid to the gaseous state. It is an indication of the volatility of a substance. The distillation range in a separation process, the temperature at which the more volatile liquid of a mixture forms a vapor, is used for mixtures in the absence of a bp. Typical units are ^{o}C or ^{o}F.

Chemical Abstracts Service Registry Number (CAS RN): A unique identification code, up to ten digits long, assigned to each chemical registered by the Chemical Abstract Service. The CAS RN is useful when searching for information on a chemical with more than one name. Over six million chemicals have been assigned CAS RNs.

Chemical Structure: A description of how atoms in a chemical are connected and arranged, including types of bonds between atoms.

Corrosivity: As defined by EPA (40 CFR 261.22), a solid waste exhibits the characteristic of corrosivity if: (1) it is aqueous and has a pH less than or equal to 2 or greater than or equal to 12.5, as determined by a pH meter using an EPA test method (Method 9049 in EPA Publication SW-846); (2) it is a liquid and corrodes steel at a rate greater than 6.35 mm (0.250") per year when tested at 55 ^{o}C as determined by the test method specified in the National Association of Corrosion Engineers Standard TM-01-69 as standardized in EPA Publication SW-846. As defined by OSHA (29 CFR 1910.1200), a chemical is corrosive if it causes visible destruction of, or irreversible alternation in living tissue by chemical action at the site of contact.

Density: The mass of a liquid, solid, or gas per unit volume of that substance, i.e., the mass in grams contained in 1 cubic centimeter (1 ml) of a substance at 20 ^{o}C and 1 atmosphere pressure. Typical units are g/ml or lbs/in^3.

Explosive: As defined by OSHA (29 CFR 1910.1200), a chemical that causes a sudden, almost instantaneous release of pressure, gas, and heat when subjected to sudden shock, pressure, or high temperature.

Flammable: As defined by OSHA (29 CFR 1910.1200), a chemical that falls into one of the following categories:

- Flammable aerosol: An aerosol that, when tested by the method described in 16 CFR 1500.45, yields a flame projection exceeding 18 inches at full valve opening, or a flashback (a flame extending back to the valve) at any degree of valve opening.
- Flammable gas:
  - A gas that, at ambient temperature and pressure, forms a flammable mixture with air at a concentration of 13 percent by volume or less; or
  - A gas that, at ambient temperature and pressure, forms a range of flammable mixtures with air wider than 12 percent by volume, regardless of the lower limit.
- Flammable liquid: Any liquid having a flashpoint below 100 ^{o}F (37.8 ^{o}C), except any mixture having components with flashpoints of 100 ^{o}F (37.8 ^{o}C) or higher, the total of which make up 99 percent or more of the total volume of the mixture.
- Flammable solid: A solid, other than a blasting agent or explosive as defined in 29 CFR 1910.109(a), that is liable to cause fire through friction, absorption of moisture, spontaneous chemical change, or retained heat from manufacturing or processing, or which can be ignited readily and when ignited burns so vigorously and persistently as to create a serious hazard. A chemical shall be considered to be a flammable solid if, when tested by the method described in 16 CFR 1500.44, it ignites and burns with a self-sustained flame at a rate greater than one-tenth of an inch per second along its major axis.

Flash Point: As defined by OSHA (29 CFR 1910.1200), the minimum temperature at which a liquid gives off a vapor in sufficient concentration to ignite when tested as follows:

- Tagliabue Closed Tester: (see American National Standard Method of Test for Flash Point by Tag Closed Tester, Z11.24-1979 [ASTM D 56-79]) for liquids with a viscosity of less than 45 Saybolt Universal Seconds (SUS) at 100 ^{o}F (37.8 ^{o}C), that do not contain suspended solids and do not have a tendency to form a surface film under test.
- Pensky-Martens Closed Tester: (see American National Standard Method of Test for Flash Point by Pensky-Martens Closed Tester, Z11.7-1979 [ASTM D 93-79]) for liquids with a viscosity equal to or greater than 45 SUS at 100 ^{o}F (37.8 ^{o}C), or that contain suspended solids, or that have a tendency to form a surface film under test.
- Setaflash Closed Tester: (see American National Standard Method of Test for Flash Point by Setaflash Closed Tester [ASTM D 3278-78].) Typical units are ^{o}C or ^{o}F.

Melting Point (mp): The temperature at which a substance changes from the solid to the liquid state. It indicates the temperature at which solid substances liquefy. Typical units are ^{o}C or ^{o}F.

Molecular Weight (MW): A summation of the individual atomic weights based on the numbers and kinds of atoms present in a molecule of a chemical substance. For polymers, this may include molecular weight distributions or average number MW (MW_n), ranges, and averages. Typical units are g/mole, daltons, or lbs/mole.

Physical State: Describes a chemical substance as a gas, liquid, or solid under ambient or other given conditions.

Reactivity: As defined by EPA (40 CFR 261.23), a solid waste is considered reactive if it exhibits any of the following properties: (1) is normally unstable and readily undergoes violent change without detonating; (2) reacts violently or forms potentially explosive mixtures with water; (3) when mixed with water, generates toxic gases, vapors, or fumes in a quantity that can present a danger to human health or the environment; (4) is a cyanide or sulfide bearing waste which, when exposed to a pH between 2 and 12.5, can generate toxic gases, vapors, or fumes in a quantity that can present a danger to human health in the environment; (5) is capable of detonation or explosive reaction if subjected to a strong initiating source or if heated under confinement; (6) is readily capable of detonation or explosive decomposition or reaction at standard temperature and pressure; or (7) is a forbidden Class A or Class B explosive as defined by the Department of Transportation (49 CFR 173). As defined by OSHA (29 CFR 1910.1200), water-reactive means a chemical will react with water to release a gas that is either flammable or presents a health hazard.

Vapor Pressure (Pv): The pressure exerted by a chemical in the vapor phase in equilibrium with its solid or liquid form. It provides an indication of the relative tendency of a substance to volatilize from the pure state. Typical units are mm Hg, torr, or in. Hg.

Water Solubility (S): The maximum amount of a chemical that can be dissolved in a given amount of pure water at standard conditions of temperature and pressure. Typical units are mg/L, g/L, or lbs/gal.

APPROACH/METHODOLOGY: The following presents a summary of the approach or methodology for obtaining chemical properties data. Methodology details for Step 6 are presented in the next section of this module.

Step 1: Prepare a list of chemical names from the substitutes tree, the Industry and Use Cluster Profile, and other pertinent documents as chemicals are identified (e.g., by the Performance Assessment or Workplace Practices & Source Release Assessment modules).

Step 2: Obtain the CAS RN and the chemical structure for each chemical on the list and identify synonyms. This will expedite the search for data on chemical properties. (Refer to Tables 5-2, 5-3, and 5-4.)

Step 3: Determine the appropriate name to be used to identify the chemical from the synonyms.

Step 4: Collect measured and/or estimated data for all of the terms listed in the Definition of Terms, when applicable. Many sources of data can be searched by CAS RN. Data are generally available from suppliers of the chemicals. (See material safety data sheets [MSDSs], described in the Process Safety Assessment module.)

Step 5: Use standard or accepted mathematical models or computer programs to estimate the data. (See Table 5-2: Mathematical Models Used to Estimate Chemical Properties.)

Step 6: Provide pertinent chemical properties to the appropriate modules (see Methodology Details below).

METHODOLOGY DETAILS: This section presents the methodology details for completing Step 6 in the above section.

Details: Step 6, Providing Pertinent Chemical Properties to the Appropriate Modules

Table 5-1 lists examples of data that the Chemical Properties module transfers to other modules in a CTSA.

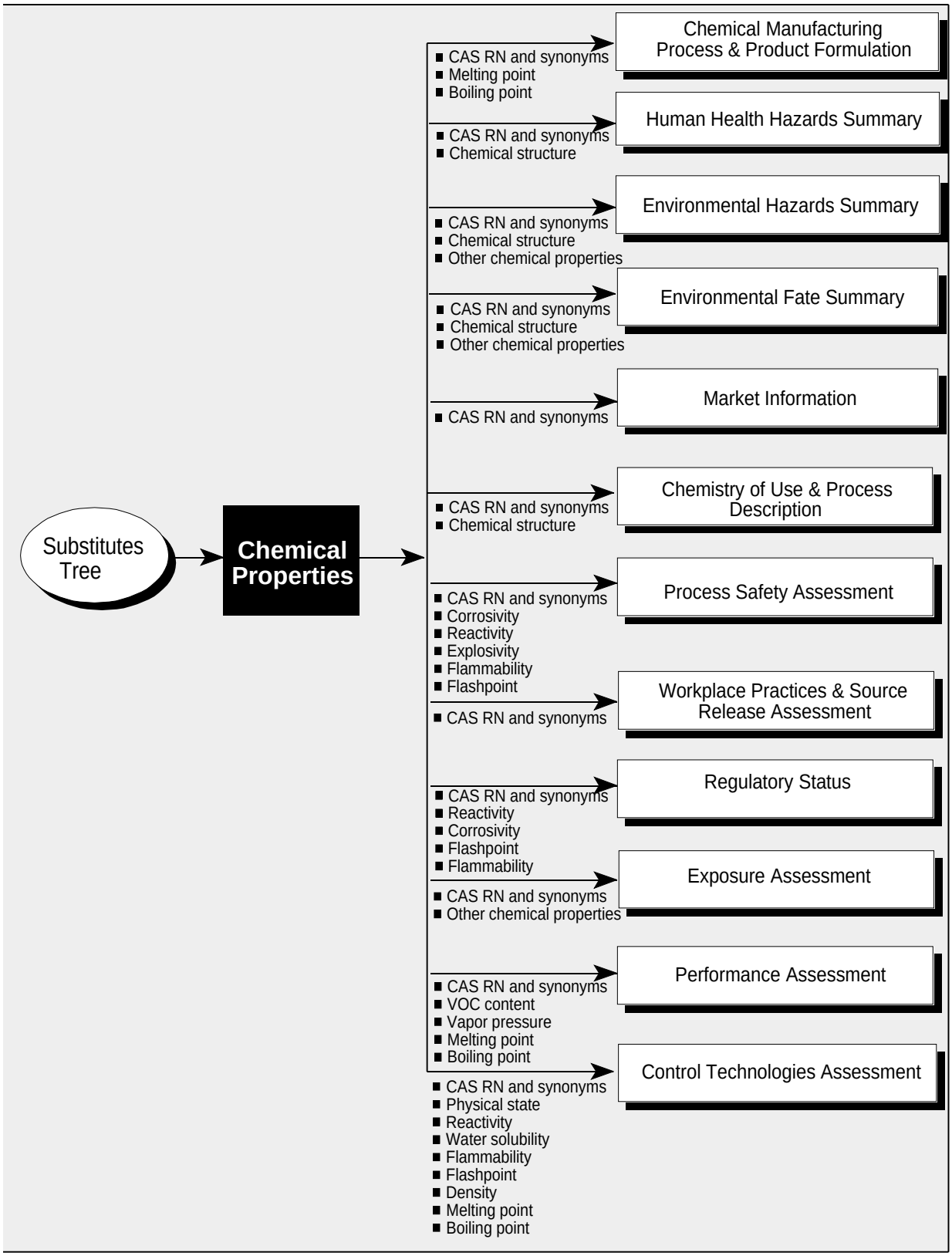
TABLE 5-1: DATA TRANSFERRED FROM THE CHEMICAL PROPERTIES MODULE

Module	Data Transferred
Chemical Manufacturing Process & Product Formulation	CAS RN, synonyms, mp, bp
Human Health Hazards Summary	CAS RN, synonyms, chemical structure
Environmental Hazards Summary	CAS RN, synonyms, chemical structure, S.

TABLE 5-1: DATA TRANSFERRED FROM THE CHEMICAL PROPERTIES MODULE	
Module	**Data Transferred**
Environmental Fate Summary	CAS RN, synonyms, chemical structure, Pv, S, mp, bp, physical state, MW
Market Information	CAS RN, synonyms
Chemistry of Use & Process Description	CAS RN, synonyms, chemical structure
Process Safety Assessment	CAS RN, synonyms, corrosivity, reactivity, explosivity, flammability, flashpoint
Workplace Practices & Source Release Assessment	CAS RN, synonyms
Regulatory Status	CAS RN, synonyms, reactivity, flammability, flashpoint, corrosivity
Exposure Assessment	CAS RN, synonyms, chemical structure, Pv, S, physical state
Performance Assessment	CAS RN, synonyms, Pv, bp, flashpoint
Control Technologies Assessment	CAS RN, synonyms, physical state, reactivity, S, flammability, flash point, mp, bp, density

FLOW OF INFORMATION: The Chemical Properties module is the basic starting point for many of the other modules in the CTSA. The Chemical Properties module receives chemical names from the substitutes tree and other sources and transfers data to the Chemical Manufacturing Process & Product Formulation, Human Health Hazards Summary, Environmental Hazards Summary, Environmental Fate Summary, Market Information, Chemistry of Use & Process Description, Process Safety Assessment, Workplace Practices & Source Release Assessment, Regulatory Status, Exposure Assessment, Performance Assessment, and Control Technologies Assessment modules. Example information flows are shown in Figure 5-1.

FIGURE 5-1: CHEMICAL PROPERTIES MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: Table 5-2 presents references for analytical models that can be used to estimate chemical properties.

TABLE 5-2: MATHEMATICAL MODELS USED TO ESTIMATE CHEMICAL PROPERTIES

Reference	Type of Model
Hunter, R.S. and F.D. Culver. 1992. *MicroQSAR Version 2.0: A Structure-Activity Based Chemical Modeling and Information System.*	Personal computer-based system of models. Uses quantitative structure-activity relationships to estimate chemical properties and aquatic toxicity values.
Syracuse Research Corporation (SRC). Continually Updated. Estimation Programs Interface (EPI©).	A shell program used to access a series of models used to estimate S, mp, bp, Pv, and environmental fate properties.
Syracuse Research Corporation (SRC). Updated Periodically. MPBVP©.	This program estimates the mp, bp, and Pv of organic compounds.

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

PUBLISHED GUIDANCE: Table 5-3 presents a reference for published guidance on chemical and physical properties and the use of estimation models for these properties.

TABLE 5-3: REFERENCES FOR CHEMICAL AND PHYSICAL PROPERTIES

Reference	Type of Guidance
Lyman, W.J., et. al. 1990. *Handbook of Chemical Property Estimation Methods.*	Methods for estimating density, Pv, S, and other chemical properties relevant to the Chemical Properties module.

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

DATA SOURCES: Table 5-4 lists sources of chemical and physical property data.

TABLE 5-4: SOURCES OF CHEMICAL AND PHYSICAL PROPERTIES DATA

Reference	Type of Data
Aldrich Chemical Company, Inc. 1990. *Catalog Handbook of Fine Chemicals*.	Commercial catalog containing over 27,000 organic and inorganic chemicals (mostly for research and development). Entries list the chemical name, CAS RN, structure, MW, and possibly the mp or bp, density, refractive index, a Beilstein reference, and other data (e.g., "hygroscopic, irritant, or moisture sensitive").
Beilstein. Beilstein on-line data base. Updated Periodically.	Data base containing data on known organic compounds. Its unique feature is its ability to define reactants in products. It is an extensive collection of physical properties and chemical reactions.
Buckingham, J. 1982. *Dictionary of Organic Compounds*.	Five volume set (plus supplements) with molecular formula and name index. Lists, with references, synthesis, spectra, physical properties, and derivatives for a large number of organic compounds.
Chemical Abstracts Systems. 1994.	Data base containing CAS RNs and chemical and physical properties.
Farm Chemicals Handbook '87. 1987.	A commercial "magazine" of registered agricultural herbicides, fungicides, and pesticides. Contains measured values of Pv, S, and many others. Usually listed by the agricultural trade name.
Handbook of Chemistry and Physics (CRC). 1992-1993.	Handbook containing CAS RNs and chemical and physical properties.
Hawley, Gessner G., et. al., Ed. 1981. *Condensed Chemical Dictionary*.	A compendium of technical data and descriptive information covering many thousands of chemicals, including their industrial uses. Also includes trademark names.
HSDB®. Hazardous Substances Data Bank (HSDB). Updated Periodically.	On-line data base containing CAS RNs, synonyms, and chemical and physical properties.
Merck Index. 1989.	Handbook containing chemical and physical properties and CAS RNs.
Perry's Chemical Engineering Handbook. 1984.	Handbook containing chemical and physical data.

TABLE 5-4: SOURCES OF CHEMICAL AND PHYSICAL PROPERTIES DATA

Reference	Type of Data
RTECS®. Registry of Toxic Effects of Chemical Substances. 1995.	An on-line data base that contains chemical identity information such as chemical name, CAS RN, synonyms, molecular formula, MW, and others. Also included are toxicity and mutagenicity information.
Sax, N. Irving and Richard J. Lewis, Sr. 1987. *Hazardous Chemicals Desk Reference*.	Handbook containing CAS RNs and chemical and physical properties as well as synonyms, hazard ratings, and current standards for exposure limits.
Syracuse Research Corporation (SRC). 1994. Environmental Fate Data Bases (EFDB©).	Data base containing CAS RNs and chemical and physical property information.
Syracuse Research Corporation (SRC). Updated Periodically. Water Solubility Data Base.	A compilation of measured S data, as well as data on other physical property values for over 4,000 (and growing) chemicals stored on a searchable computer data base (ChemBase v.1.4). It currently contains referenced data from the Arizona data base, the Syracuse data base, the Merck Index, on-line Beilstein, other pertinent literature, and journal articles.
U.S. Department of Health and Human Services. 1985. CHEMLINE: Chemical Dictionary Online.	An on-line interactive chemical dictionary file containing one million chemical substance records. The data elements consist of CAS RNs, molecular formula, synonyms, ring information (part of the structure of some chemicals), and a locator to other on-line data bases that would contain further information on that compound.
U.S. Environmental Protection Agency. 1995d. *Integrated Risk Information System (IRIS®).*	An on-line data base that contains information and data on numerous chemical substances. Information includes substance identification (name and CAS RN) and physical properties such as color/form, odor, bp, mp, MW, density, vapor density, Pv, solubilities, flash point, and others.
Verschueren, K. 1983. *Handbook of Environmental Data on Organic Chemicals.*	An extensive text compiling information on organic chemicals. The data given include formula, physical appearance, MW, mp, bp, Pv, and solubility.

TABLE 5-4: SOURCES OF CHEMICAL AND PHYSICAL PROPERTIES DATA	
Reference	**Type of Data**
Worthing, Charles R. and S. Barrie Walker. 1987. *Pesticide Manual*.	An index of agricultural pesticides which contains chemical names and physical properties, such as mp or bp, Pv, S, and other useful measured values.

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

CHEMICAL MANUFACTURING PROCESS & PRODUCT FORMULATION

OVERVIEW: Chemical manufacturing is the process through which a chemical is synthesized from raw materials or other chemical feedstocks. Product formulation is the process by which chemical products, composed of one or more ingredients, are prepared according to the product formula. This module: (1) describes the process for manufacturing the chemicals in the use cluster; and (2) describes the chemical product formulation process, if applicable. In both cases, the descriptions focus on the industrial or laboratory means of synthesis, the necessary starting materials and feedstocks, by-products and co-products, isolated or non-isolated intermediates, and relevant reaction conditions (e.g., temperature, pressure, catalyst, solvents, and other chemicals).

GOALS:

- Describe the processes for manufacturing chemicals in the use cluster.
- Describe the process for formulating chemical products used in the use cluster, if applicable.
- Compile chemical manufacturing and product formulation data to be used by subsequent modules if the impacts of these up-stream processes are being evaluated in a CTSA.

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

- Knowledge of chemical feedstocks, synthetic chemical reaction catalysts, and reaction conditions.
- Understanding of chemical manufacturing processes, including both batch and continuous processes, as well as chemical equilibria, kinetics, and heat and mass transfer.

Within a business or DfE project team, the people who might supply these skills include a chemist and a chemical or process engineer. Vendors of the chemicals or chemical formulations may also be a good resource.

DEFINITION OF TERMS:

Catalyst: A substance that accelerates a chemical reaction but which itself is not consumed in the reaction.

Chemical By-product: An unintended chemical compound that is formed by a chemical reaction.

Chemical Intermediate: A chemical substance that is formed during the reaction and then undergoes further reaction to produce a product.

Chemical Product: In a CTSA, refers to products in the use cluster composed of one or more chemicals for which product formulation data must be obtained.

Chemical Reaction: The process that converts a substance into a different substance.

Feedstock: A raw material, pure chemical, or chemical compound that is used to synthesize a chemical.

Unit Operation: A process step that achieves a desired function.

APPROACH/METHODOLOGY: The following presents a summary of the approach or methodology for describing the chemical manufacturing processes and product formulation methods of chemicals or chemical products. Methodology details for Steps 3, 4, and 9 follow this section.

Chemical Manufacturing

Step 1: Obtain chemical information, including CAS RNs, synonyms, melting points, and boiling points from the Chemical Properties module.

Step 2: Determine the primary industrial mode of synthesis for each chemical in the use cluster (refer to data sources in Table 5-5).

Step 3: Develop a chemical manufacturing process flow diagram for the primary mode of synthesis. The diagram should identify the major unit operations and equipment, as well as all input and output streams (see Methodology Details for an example chemical manufacturing process description).

Step 4: Identify any chemical intermediates, catalysts, feedstocks, and chemical products or by-products involved in the synthesis that have the potential for release.

Product Formulation

Step 5: Obtain chemical product formulation data for any chemical products being evaluated in the CTSA from the Performance Assessment module. When proprietary chemical products are being used, only generic formulations may be available.

Step 6: Determine the primary industrial method of formulation for each chemical product being evaluated. Mixing operations, with or without the addition of heat or pressure, are typical manufacturing processes for product formulations.

Step 7: Develop a process flow diagram for the primary industrial method of formulation. The diagram should include the unit operations, material flows, and equipment used in the formulation process. If a chemical reaction occurs in the formulation process, determine if any special reaction conditions are required (e.g., the presence of heat, cooling, a catalyst, etc.). If a product is formulated by mixing only (e.g., does not involve chemical reactions), determine if any special conditions (e.g., heat, pressure, etc.) are required to get ingredients into solution. This information can be used to evaluate the energy impacts of the alternatives.

Step 8: Identify any chemical intermediates, catalysts, feedstocks, and chemical products or by-products involved in the product formulation process that have the potential for release.

Transferring Information

Step 9: Provide the following information to the modules listed below:

- Energy usage resulting from the chemical manufacturing and product formulation processes (e.g., heat, pressure, etc.) to the Energy Impacts module.
- Material streams usage resulting from the chemical manufacturing or product formulation processes (e.g., chemical feedstocks, catalysts, etc.) to the Resource Conservation module.

METHODOLOGY DETAILS: This section presents the methodology details for completing Step 3, 4, and 9 from the Chemical Manufacturing section above.

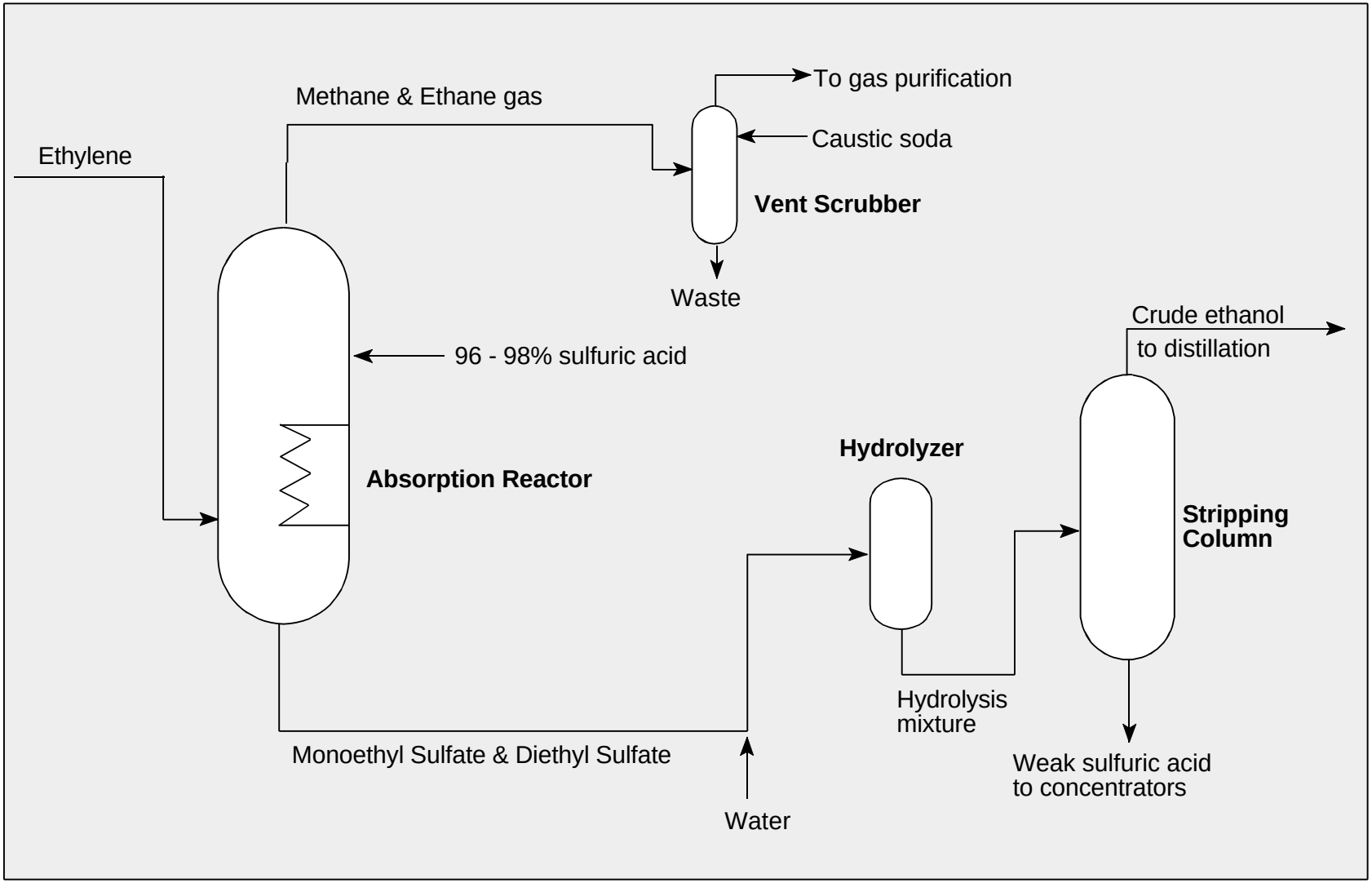
Details: Steps 3 and 4, Example Description of Chemical Manufacturing Process

The following description of the synthetic preparation of ethanol by indirect hydration is an example of the chemical manufacturing process description developed in Steps 3 and 4. The process information was gathered from the data sources listed in the Table 5-5.

Indirect Hydration of Ethanol

The preparation of ethanol from ethylene using sulfuric acid is a three step hydration process as discussed below. A flow diagram for this process is shown in Figure 5-2.

FIGURE 5-2: PROCESS FLOW DIAGRAM FOR THE MANUFACTURE OF ETHANOL BY INDIRECT HYDRATION



Step 1: Formation of monoethyl sulfate and diethyl sulfate by the absorption of ethylene in concentrated sulfuric acid.

$$\underset{\text{(Ethylene)}}{CH_2 = CH_2} + \underset{\text{(Sulfuric Acid)}}{H_2SO_4} \rightarrow \underset{\text{(Monoethyl Sulfate)}}{CH_3CH_2OSO_3H}$$

$$\underset{\text{(Ethylene)}}{2\ CH_2 = CH_2} + \underset{\text{(Sulfuric Acid)}}{H_2SO_4} \rightarrow \underset{\text{(Diethyl Sulfate)}}{(CH_3CH_2O)_2SO_2}$$

Step 2: Formation of ethanol by hydrolysis of ethyl sulfates.

$$\underset{\text{(Monoethyl Sulfate)}}{CH_3CH_2OSO_3H} + \underset{\text{(Water)}}{H_2O} \rightarrow \underset{\text{(Ethanol)}}{CH_3CH_2OH} + \underset{\text{(Sulfuric Acid)}}{H_2SO_4}$$

$$\underset{\text{(Diethyl Sulfate)}}{(CH_3CH_2O)_2SO_2} + \underset{\text{(Water)}}{2\ H_2O} \rightarrow \underset{\text{(Ethanol)}}{2\ CH_3CH_2OH} + \underset{\text{(Sulfuric Acid)}}{H_2SO_4}$$

$$\underset{\text{(Diethyl Sulfate)}}{(CH_3CH_2O)_2SO_2} + \underset{\text{(Ethanol)}}{CH_3CH_2OH} \rightarrow \underset{\text{(Monoethyl Sulfate)}}{CH_3CH_2OSO_3H} + \underset{\text{(Diethyl Ether)}}{(CH_3CH_2)_2O}$$

Step 3: Reconcentration of the dilute sulfuric acid.

The primary input streams for this process are the hydrocarbon feedstock containing 35-95 percent ethylene, methane, and ethane; 96-98 percent sulfuric acid, and water.

The adsorption is carried out in a column reactor at 80 ^{o}C and 1.3-1.5 MPa of pressure where the ethylene feedstock is adsorbed in an exothermic reaction with the sulfuric acid. The column is cooled to reduce the reaction temperature and to limit corrosion problems. The hydrolysis of the ethyl sulfates in the second step of the process is done using just enough water to produce a 50-60 percent sulfuric acid solution. The resulting mixture is separated by a stripping column to yield sulfuric acid and a gaseous mixture of alcohol, ether, and water. The gaseous mixture is mixed with water and then distilled until pure. Finally, the sulfuric acid is then reconcentrated using a reboiler and a two stage vacuum evaporation system until the concentration is above 90 percent.

The primary output streams and by-products of this reaction are the following:

- Ethanol (product).
- Dilute 50-60 percent sulfuric acid.
- Scrubber waste containing the unreacted methane and ethane as well as any other gases present.
- Diethyl ether (by-product).

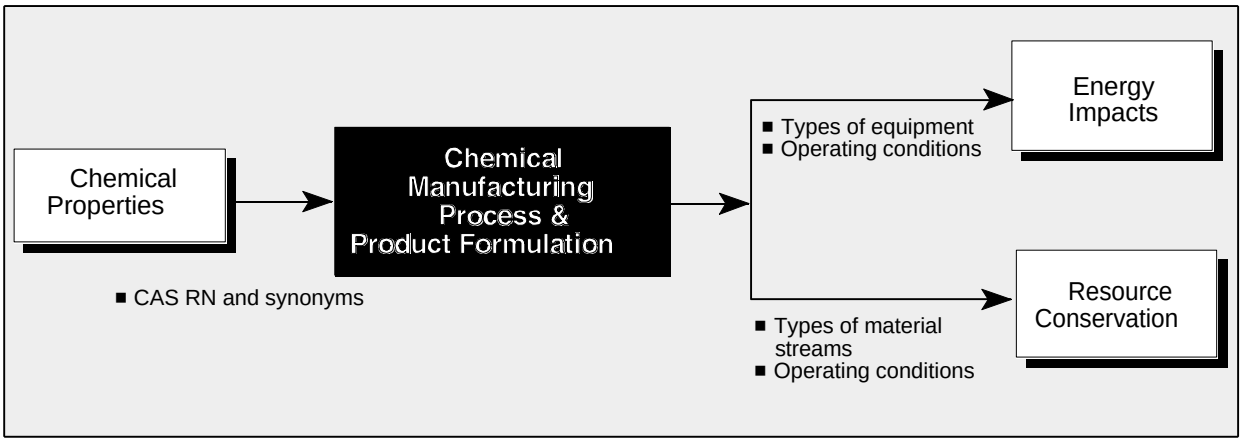
The intermediate compounds of monoethyl sulfate and diethyl sulfate are also present, although they are not waste streams, because they are consumed by the process.

Details: Step 9, Transferring Information

Past CTSAs have not quantitatively evaluated the chemical manufacturing and product formulation processes. Instead, attention has focussed on the relative effects of up-stream processes on energy and other resources consumption. If the effects of up-stream processes on human health and environmental risks are being quantified in a CTSA, the identities of chemical intermediates, catalysts, feedstocks, and chemical products or by-products are transferred to the Chemical Properties module and other modules that ultimately feed into the risk characterization. Process flow diagrams are transferred to the Workplace Practices & Source Release Assessment module.

FLOW OF INFORMATION: In a CTSA, this module receives information from the Chemical Properties module and transfers information, if desired, to the Energy Impacts and Resource Conservation modules. Example information flows are shown in Figure 5-3. This module could also transfer information to other modules if these processes are being fully and quantitatively evaluated. For example, chemical intermediates released during chemical manufacturing process could be evaluated in the hazards summary modules.

FIGURE 5-3: CHEMICAL MANUFACTURING PROCESS & PRODUCT FORMULATION MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: None cited.

DATA SOURCES: Table 5-5 lists data sources for both chemical manufacturing processes and product formulation methods.

TABLE 5-5: SOURCES OF CHEMICAL MANUFACTURING PROCESS AND PRODUCT FORMULATION INFORMATION

Reference	Type of Data
HSDB®. Hazardous Substance Data Bank (HSDB). Updated Periodically.	Contains brief summaries of chemical manufacturing processes.
Kirk-Othmer Encyclopedia of Chemical Technology. Updated Periodically.	Comprehensive source of chemical synthesis processes.
Ullmann, Fritz. 1985. *Ullmann's Encyclopedia of Industrial Chemistry*.	Comprehensive source of chemical synthesis processes.

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

ENVIRONMENTAL FATE SUMMARY

OVERVIEW: The environmental fate of chemicals describes the processes by which chemicals move and are transformed in the environment. Environmental fate processes that should be addressed include: persistence in air, water, and soil; reactivity and degradation; migration in groundwater; removal from effluents by standard waste water treatment methods; and bioaccumulation in aquatic or terrestrial organisms.

Note: There is no single accepted methodology for evaluating the environmental behavior of chemicals; this is particularly true in the selection of mathematical models to predict environmental fate parameters. Thus it is important to document the approach and specific procedures used in the module. The approach presented below is one suggested by the types of information included in recent EPA Risk Management Reports.

GOALS:

- Retrieve data or estimate key environmental fate parameters for each chemical in the use cluster.
- Prepare environmental fate and treatability summaries for each chemical.
- Provide data to the Human Health Hazards Summary, Environmental Hazards Summary, Exposure Assessment, and Control Technologies Assessment modules.

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

- Knowledge of the physical, chemical, and biological reactions of chemicals in the environment.
- Knowledge of standard waste water treatment systems and unit processes.
- Experience with the use of mathematical models for predicting the fate and transformation of chemicals in the environment.

Note: The analysis described in this module should only be undertaken by someone familiar with environmental fate calculations. Furthermore, peer-review of the completed environmental fate summary is recommended.

DEFINITION OF TERMS: Several terms from the Chemical Properties module are also used in the Environmental Fate Summary module and are defined here as well.

Chemical Properties

Vapor Pressure (Pv): The pressure exerted by a chemical in the vapor phase in equilibrium with its solid or liquid form. It provides an indication of the relative tendency of a substance to volatilize from the pure state. Typical units are mm Hg, torr, or in. Hg.

Water Solubility (S): The maximum amount of a chemical that can be dissolved in a given amount of pure water at standard conditions of temperature and pressure. Typical units are mg/L, g/L, or lbs/gal.

Environmental Fate

Atmospheric Residence Time (τ): The ratio of the total mass of a chemical in an atmospheric compartment to either the total emission rate or the total removal rate, under steady-state conditions. Units are typically in hours or days.

Biochemical Oxygen Demand (BOD): The amount of oxygen consumed by microorganisms, over a specified time period, to metabolize a substance. Under certain environmental conditions, a high BOD may result in a reduction in oxygen levels in receiving waters to below critical levels for sustaining aquatic life.

Bioconcentration Factor (BCF): The equilibrium ratio of the concentration of a chemical in an exposed organism to the concentration of the chemical in the surrounding water.

Biodegradation: The transformation of chemical compounds by living organisms. Not confined to microorganisms (e.g., bacteria, fungi) but chiefly a microbial process in nature; typically expressed in terms of a rate constant and/or half-life.

Chemical Oxygen Demand (COD): The amount of oxygen consumed in the oxidation of a chemical substrate by a strong chemical oxidant (such as dichromate).

Half-life ($t_{½}$): The time required to reduce the concentration of a chemical to 50 percent of its initial concentration. Units are typically in hours or days.

Henry's Law Constant (H_c): The air/water partition coefficient, describing the relative concentrations of a chemical in air (the vapor phase) and the chemical dissolved in water, in a closed system at equilibrium. H_c can be measured directly or estimated as the ratio of Pv to S, and gives an indication of a chemical's tendency to volatilize from water to air or dissolve into water from air. H_c is typically expressed in units of atm-m^3/mole or in dimensionless terms.

Hydrolysis: A chemical transformation process in which a chemical reacts with water. In the process, a new carbon-oxygen bond is formed with oxygen derived from the water molecule, and a bond is cleaved within the chemical between carbon and some functional group.

Hydroxyl Radical Rate Constant (K_{OH}): The rate constant (in cm^3/mol/sec) for the reaction of photochemically produced hydroxyl radicals with organic compounds in the atmosphere.

Ionization or Acid Dissociation Constant (K_a, pK_a): An equilibrium ratio of the dissociation products and the parent compound in aqueous solutions. The degree of dissociation can alter the solubility and adsorption characteristics of the compound. The pK_a is the negative log of K_a.

Mobility: The tendency for a chemical to move in the environment (i.e., through soil with the percolation of water).

Octanol-Water Partition Coefficient (K_{ow}): The equilibrium ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system, typically expressed in log units (log K_{ow}). K_{ow} provides an indication of a chemical's S, fat solubility (lipophilicity), its tendency to bioconcentrate in aquatic organisms, and to sorb to soil or sediment.

Organic Carbon Partition Coefficient (K_{oc}): The proportion of a chemical sorbed to the solid phase, at equilibrium in a two-phase, water/soil or water/sediment system expressed on an organic carbon basis. Chemicals with higher K_{oc} values are more strongly sorbed and, therefore, tend to be less mobile in the environment.

Oxidation: In general, a reaction in which electrons are transferred from a chemical to an oxidizing agent, or where a chemical gains oxygen from an oxidizing agent. (Also see Redox and Reduction.)

Percent Removal: The amount of the chemical that can be removed from sewage by standard waste water treatment processes, expressed in terms of the percent of the initial amount removed from the influent (liquid) waste stream. The chief processes that may contribute to removal from a liquid waste stream are degradation (biotic or abiotic), sorption, and volatization (also known as air stripping).

Persistence: The ability of a chemical substance to remain in a particular environment in an unchanged form.

Photolysis: The transformation of a chemical by light energy.

Plant Uptake: The uptake of a chemical into plants is expressed in terms of a bioconcentration factor for vegetation (B_v), which is the ratio of the concentration in the plant tissue to the concentration in soil.

Redox: Reduction-oxidation reactions. Oxidation and reduction occur simultaneously; in general, the oxidizing agent gains electrons in the process (and is reduced) while the reducing agent donates electrons (and is oxidized).

Reduction: In general, a reaction in which electrons are transferred to a chemical from a reducing agent, or where oxygen is removed from a chemical. (Also see Oxidation and Redox.)

Soil or Sediment Sorption Coefficient (K_d): The equilibrium ratio between a chemical sorbed to the solid phase and in solution in a two-phase, soil/water or sediment/water system.

Smog-Forming Potential: The chemical reaction of hydrocarbons to produce atmospheric photochemical oxidants such as ozone and other by-products contributing to the formation of smog.

Transport: The movement of a chemical through the environment, within a single phase or from one phase to another.

Treatability: The amenability of a chemical substance or waste stream to removal during waste water treatment, without adversely affecting the normal operation of the treatment plant.

Ultraviolet (UV): That part of the electromagnetic spectrum at a frequency higher than visible light (corresponding to wavelengths of 3000-4000 Å).

Volatilization: The transport process by which a chemical substance enters the atmosphere by evaporation from soil or water.

ADDITIONAL TERMS: The following additional terms are not used in this module discussion *per se*, but are likely to be found in the literature pertaining to chemical fate parameters.

Acclimation: The process in which continuous exposure of a microbial population to a chemical results in a more rapid transformation (biodegradation) of the chemical than initially observed.

Activated Sludge: The flocculated mixture of microorganisms and inert organic and inorganic material normally produced by aeration of sewage. Constitutes the biological treatment process most frequently employed for purification of domestic sewage.

BOD/COD Ratio: The ratio of the BOD to the COD for a chemical mixture.

Direct Aqueous Photolysis Rate Constant (k_d): The rate constant (in day^{-1} or $year^{-1}$) for the direct photolytic transformation of an organic compound in water.

Ozone Rate Constant(k_{O3}): The rate constant (cm^3/mol/sec) for the reaction of ozone with an organic compound.

Photooxidation: A process in which solar radiation generates an oxidizing agent, such as the hydroxyl radical, which reacts with (and transforms) a chemical.

Wet Deposition: The process by which a chemical that is dissolved in water in the atmosphere reaches land or a water body via precipitation (synonym: atmospheric washout).

APPROACH/METHODOLOGY: The following outlines the technical approach or methodology for preparing an environmental fate summary. Further methodology details for Steps 3 and 4 follow this section.

Step 1: Obtain CAS RNs and synonyms, information on chemical structure, and physical and chemical properties of the chemicals in the use cluster from the Chemical Properties module.

Step 2: Obtain measured or estimated environmental fate and treatability data for each chemical from primary and secondary sources (see Table 5-7: Sources of Environmental Fate Data).

Step 3: If environmental fate and treatability data are not available, estimate parameters using regression equations and mathematical models (see Details: Step 3, below).

Step 4: Prepare environmental fate and treatability summaries for each chemical, focussing on water, air, soil and waste water treatment environments as appropriate. Fate summaries should focus on the fate processes that are most important for that particular chemical. (See Details: Step 4, below.)

Step 5: Provide environmental fate summaries and environmental fate parameter values, and identify any products of chemical degradation (if applicable) to the Human Health Hazards Summary, Environmental Hazards Summary, and Exposure Assessment modules; and provide treatability parameters (e.g., percent removal), environmental fate, and treatability summaries to the Control Technologies Assessment module.

METHODOLOGY DETAILS: This section presents methodology details for completing Steps 3 and 4, and examples of environmental fate and treatability summaries. If necessary, additional information on these and other steps can be found in the previously published guidance.

Details: Step 3, Estimating Environmental Fate Parameters

Numerous mathematical models, such as regression equations, have been developed for estimating environmental parameters for chemicals. Only a few examples will be presented here; many others exist, and the ones most appropriate for a given chemical will depend on the circumstances. Published guidance should be consulted for selecting specific methods and equations.

The K_{oc} of a chemical can be estimated from K_{ow}, from S or from BCF, for example:

$$\log K_{oc} = 0.544 \log K_{ow} + 1.377$$

$$\log K_{oc} = -0.55 \log S + 3.64$$

$$\log K_{oc} = 0.681 \log BCF + 1.963$$

The τ for a chemical can be estimated from the rate at which the chemical reacts with hydroxyl radicals, for example:

$$\tau_{OH\cdot} = 1/\{K_{OH} [OH\cdot]\}$$

where:

K_{OH} is in liters/mole/sec and [OH·] is in units of moles/liter

The bioconcentration of a chemical in aquatic species can be estimated from the chemical's octanol-water partition coefficient (K_{ow}), for example:

$$\log BCF = 0.76 \log K_{ow} - 0.23$$

Details: Step 4, Preparing Environmental Fate and Treatability Summaries

Examples of environmental fate and treatability summaries (from the Screen Printing CTSA) for acetone and dichloromethane are shown below:

Environmental Fate Summary for Acetone

If released on soil, acetone will volatilize into the air or leach into the ground where it will probably biodegrade. Photolysis will be important on terrestrial surfaces and in surface waters exposed to sunlight. If released to water, acetone may also be lost due to volatilization (estimated $t_{½}$ is 20 hours from a model river) and biodegradation. Bioconcentration in aquatic organisms and adsorption to sediment should not be important transport processes in water. In the atmosphere, acetone will be lost by photolysis and reaction with photochemically produced hydroxyl radicals. Half-life estimates from these combined processes average 22 days and are shorter in summer and longer in winter. In air, acetone may also be washed out by rain. A rapid and a moderate biodegradation rate for acetone used in the Sewage Treatment Plant (STP) fugacity model results in 97 and 84 percent predicted total removal from waste water treatment plants, respectively.

Environmental Fate Summary for Dichloromethane

If released to soil, dichloromethane is expected to display high mobility. It may rapidly volatilize from both moist and dry soil to the atmosphere. Aerobic biodegradation may be important for dichloromethane in acclimated soils. If released to water, volatization to the atmosphere is expected to be a rapid process. Neither bioconcentration in fish and aquatic organisms, nor

adsorption to sediment and suspended organic matter are expected to be significant. Dichloromethane has been found to slowly biodegrade under aerobic conditions. It is also expected to slowly biodegrade under anaerobic conditions in sediment and groundwater. If released to the atmosphere, dichloromethane is expected to persist for long periods of time. The estimated $t_{½}$ for the gas-phase reaction of dichloromethane with hydroxyl radicals is approximately 88 days. Direct photolytic degradation is not expected to occur. Dichloromethane may undergo atmospheric removal by wet deposition processes, although any removed by this process is expected to rapidly re-volatilize to the atmosphere. Using a slow biodegradation rate for dichloromethane in the STP fugacity model, 64 percent total removal can be predicted from waste water treatment plants.

Also, Appendix H presents an example of an Initial Review Exposure Report for dichloromethane. This form shows the environmental fate data that are typically reported along with some additional chemical property and toxicity information.

Relevant Environmental Fate Properties by Environmental Medium

For each type of environment, the types of fate and property data that are likely to be most relevant are listed below.

For water, the following are likely to be the most important properties and processes which should be considered in developing an environmental fate summary:

- S.
- Volatilization (H_c, $t_{½}$).
- Adsorption to sediments and suspended particulate matter (K_{oc}, K_d).
- Photolysis ($t_{½}$).
- Hydrolysis (rate constant and $t_{½}$).
- BCF.
- Biodegradation.

For soil, the following are likely to be the most important properties and processes which should be considered in developing an environmental fate summary:

- S.
- Volatilization (H_c).
- Adsorption to organic matter (K_{oc} and K_d).
- Adsorption to inorganic matter.
- Potential for groundwater contamination.
- Potential for uptake by plants.
- Biodegradation.
- Hydrolysis.
- Photolysis on soil surfaces.

For air, the following are likely to be the most important properties and processes which should be considered in developing an environmental fate summary:

- Volatility (Pv, H_c).
- τ.
- Photolysis ($t_{½}$).
- Reactivity with hydroxyl radicals, ozone (k_{O_3}), and other oxidants.
- UV absorption.
- Smog-forming potential.
- Ozone depleting potential.
- Wet deposition.

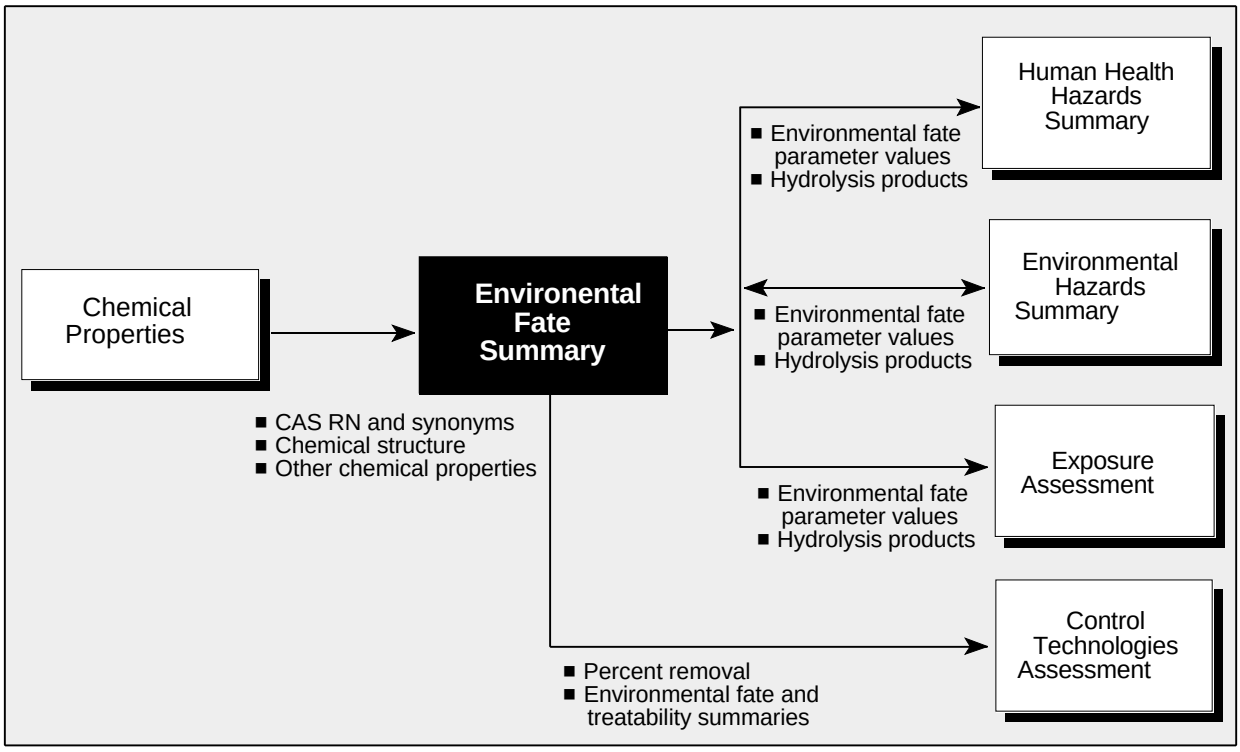
For treatability, the following are likely to be the most important properties and processes which should be considered in developing an environmental fate summary:

Environmental Fate Summary

- Biodegradability.
- Sorption potential (K_{oc}).
- Volatilization (H_c).
- Hydrolysis.

FLOW OF INFORMATION: In a CTSA, the Environmental Fate Summary module receives information from the Chemical Properties module and transfers information to the Human Health Hazards Summary, Environmental Hazards Summary, Exposure Assessment, and Control Technologies Assessment modules. Example information flows are shown in Figure 5-4.

FIGURE 5-4: ENVIRONMENTAL FATE SUMMARY MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: Environmental fate and transport modeling is performed as part of the Exposure Assessment module. Models for estimating environmental fate parameters are included in Table 5-6, below.

PUBLISHED GUIDANCE: EPA has not published comprehensive guidance on the development of environmental fate summaries. Individual program offices may utilize different approaches. Table 5-6 lists references in which methods for estimating chemical properties and environmental fate parameters are discussed.

TABLE 5-6: REFERENCES FOR ESTIMATING ENVIRONMENTAL FATE PARAMETERS

Reference	Type of Guidance
BioByte, Inc. CLOGP for Windows, Version 1.0. 1996. MACLOGP (for Macintosh computers), Version 2.0. 1996. CLOGP VAX/VMS, Version 2.10. 1996.	Mathematical models used to estimate K_{ow}. Three versions currently available (as of June, 1996).
Boethling, R.S. 1993. "Structure Activity Relationships for Evaluation of Biodegradability in the EPA's Office of Pollution Prevention and Toxics."	Describes the development, validation, and application of SARs in EPA OPPT.
Briggs, G.C. 1981. "Theoretical and Experimental Relationships between Soil Adsorption, Octanol-Water Partition Coefficients, Water Solubilities, Bioconcentration Factors, and the Parachor."	BCFs are estimated for neutral compounds from K_{ow}.
Hamrick, K.J., et. al. 1992. "Computerized Extrapolation of Hydrolysis Rate Data."	Provides estimates of hydrolysis rate constants at specific temperatures.
Hassett, J.J. 1981. "Correlation of Compound Properties with Sorption Characteristics of Nonpolar Compounds by Soils and Sediments: Concepts and Limitations."	Sorption constants for nonpolar organic compounds are correlated with S, K_{ow}, or with organic carbon content of soil or sediment.
Kollig, H.P. 1993. *Environmental Fate Constants for Organic Chemicals under Consideration for EPA's Hazardous Waste Identification Projects*.	Literature-derived data as well as model computations are used to estimate hydrolysis, adsorption, and oxidation-reduction parameters.

TABLE 5-6: REFERENCES FOR ESTIMATING ENVIRONMENTAL FATE PARAMETERS	
Reference	**Type of Guidance**
Lyman, W.J., et. al. 1990. *Handbook of Chemical Property Estimation Methods*.	Describes methods for estimating residence time, K_{ow}, K_{oc}, BCF, acid dissociation constants, hydrolysis, aqueous photolysis, biodegradation, and volatilization rates, and other chemical properties.
Mackay, D., et. al. 1992. *Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals*.	Provides physical-chemical data and fugacity calculations for organic compounds.
Meylan, W., et. al. 1992. "Molecular Topology/Fragment Contribution Method for Predicting Soil Sorption Coefficients."	Program for estimating K_{oc} based on molecular connectivity indices and structure-based correction factors.
Syracuse Research Corporation (SRC). Continually Updated. Estimation Programs Interface (EPI©).	Series of models to estimate log K_{ow}, volatilization $t_{½}$ for water, soil-sediment sorption coefficient, H_c, biodegradation, atmospheric oxidation rates, rate of hydrolysis, rate of removal in waste water treatment plants, and other chemical properties.

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

DATA SOURCES: Table 5-7 lists major sources of environmental fate data.

TABLE 5-7: SOURCES OF ENVIRONMENTAL FATE DATA	
Reference	**Type of Data**
Bedar, R.G. 1976. *Biodegradability of Organic Compounds*.	Biodegradability values for various organic compounds.
Callahan, M.A., et. al. 1979. *Water-related Environmental Fate of 129 Priority Pollutants*.	Information on environmental fate of priority pollutants in aqueous systems.
Darnall, K.R. 1986. "Reactivity Scale for Atmospheric Hydrocarbons Based on Reaction with Hydroxyl Radicals."	A classification of atmospheric chemical reactivity and potential for smog formation based on hydroxyl radical rate constants.
Farley, F. 1977. *Photochemical Reactivity Classification of Hydrocarbons and Other Organic Compounds*.	Classification for photochemical reactivity of organic compounds.
Hansch, C. and A. Leo. 1987. *The Log P Data Base*.	List of K_{ow} values.

TABLE 5-7: SOURCES OF ENVIRONMENTAL FATE DATA

Reference	Type of Data
Helfgott, T.B., et. al. 1977. *An Index of Refractory Organics*.	Biodegradability values for various organic compounds.
Hendry D.G. and R.A. Kenley. 1979. *Atmospheric Reaction Products of Organic Compounds.*	Rate constants (K_{OH}) for the reaction of organic compounds with hydroxyl radical.
Howard, P.H., et. al. 1991. *Handbook of Environmental Degradation Rates.*	Provides environmental degradation $t_{½}$ data for chemicals in soil, air, surface water and groundwater, and aerobic and anaerobic aqueous biodegradation.
HSDB®. Hazardous Substances Data Bank (HSDB). Updated Periodically.	On-line data base including measured and estimated chemical property and environmental fate parameters.
Kollig, H.P. 1993. *Environmental Fate Constants for Organic Chemicals Under Consideration for EPA's Hazardous Waste Identification Projects.*	Literature-derived data as well as model computations to estimate hydrolysis, adsorption, and oxidation-reduction parameters.
Lyman, W.J., et. al. 1974. *Survey Study to Select a Limited Number of Hazardous Materials to Define Amelioration Requirements*.	List of BOD_5/COD ratios for various organic compounds.
Mabey, W. and T. Mill. 1978. "Critical Review of Hydrolysis of Organic Compounds in Water Under Environmental Conditions."	Data on hydrolysis rate constants of organic compounds.
Mackay, D., et. al. 1992. *Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals*.	Provides physical-chemical data and fugacity calculations for organic compounds.
Pitter, P. 1976. "Determination of Biological Degradability of Organic Substances."	List of removal efficiencies and average rate of biodegradation for various organic compounds.
Reinbold, K.A., et. al. 1979. *Adsorption of Energy-Related Organic Pollutants: A Literature Review*.	Adsorption data extracted from the literature.
State of California Air Resources Board. 1986. *Adoption of a System for the Classification of Organic Compounds According to Photochemical Reactivity*.	Relative atmospheric reactivity scale.
Syracuse Research Corporation (SRC). 1994. Environmental Fate Data Bases (EFDB©).	Comprehensive on-line and personal computer-based data base containing quantitative data on environmental fate parameters.

TABLE 5-7: SOURCES OF ENVIRONMENTAL FATE DATA	
Reference	**Type of Data**
Trapp, S. 1993. "Modelling the Uptake of Organic Compounds into Plants."	Describes estimating plant-soil BCFs using a fugacity model based on the ratio of K_{ow}:K_{oc}, the lipid fraction of plants, the organic carbon and water content of the soil, and transfer and metabolism kinetics.
U.S. Environmental Protection Agency. 1974. *Proceedings of the Solvent Reactivity Conference.*	Classification of chemical reactivity for compounds associated with mobile source emissions.
U.S. Environmental Protection Agency. 1991a. *The Environmental Fate Constants Information System Database (FATE).*	Provides data on H_c, K_{ow}, K_{oc}, K_d, k_{OH}, pK_a, and oxidation-reduction reactions of organic compounds.
U.S. Environmental Protection Agency. 1994d. *Treatability Database. Version 5.0.*	Personal computer-based collection of data including H_c, K_{ow}, treatability of organic compounds, and other chemical properties.
Verschueren, K. 1983. *Handbook of Environmental Data on Organic Chemicals.*	Information derived from primary literature on environmental parameters, including treatability.

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

HUMAN HEALTH HAZARDS SUMMARY

OVERVIEW: Human health hazards assessment is the process of identifying the potential effects that a chemical may have on humans who are exposed to it, and of determining the levels at which these effects may occur. Exposure to a chemical may occur by inhalation, oral, or dermal routes through the production, use, or disposal of the chemical or products containing the chemical.

GOALS:

- Compile existing information on potential health effects resulting from exposure to a chemical.
- Guide the selection and use of chemicals that pose less risk to humans.
- Assess the potential toxicity of chemicals in a use cluster to humans from available human data, supplementing with animal data when adequate human data are not available.
- Identify the target organ(s) of toxicity by examining the potential effects resulting from acute (short-term) and chronic (long-term) exposure to the chemical by routes pertinent to human exposure.
- Determine if there are levels of concern for the chemical (e.g., the no-observed adverse effect level [NOAEL] and the lowest-observed adverse effect level [LOAEL]), as well as references doses (RfD), carcinogen slope factors (q_1*), and cancer weight-of-evidence classifications.
- Provide the above listed information, including the levels of concern, to the Risk Characterization module.

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

- Expertise in evaluating the adverse effects of chemicals on humans, animals, and other biological systems. This requires an understanding of clinical toxicology; procedures and results of standard toxicological test methods; pharmacokinetics, a discipline that includes chemical absorption, distribution, metabolism, and excretion; species differences among experimental animals; the cellular, biochemical, and molecular mechanisms of action of the chemicals; and relationships between chemical structure and toxicity.
- Expertise in analyzing data on adverse effects in human populations (in this case, from exposure to chemicals) and extracting information to identify possible causes. This

discipline requires knowledge of standard protocols for epidemiological studies; demographics; risk factors (e.g., smoking, alcohol consumption, race, sex, obesity, etc.); formal logic; and statistics.

- Expertise in the collection, organization, and interpretation of numerical data; especially the analysis of population characteristics by inference from sampling. This requires knowledge of population parameter estimation (involves a quantitative measure of some property of a sample), hypothesis testing (involves determining if differences in sample statistics [e.g., means] are of sufficient magnitude to distinguish differences between population parameters), and modeling.

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

DEFINITION OF TERMS: Sources for the following definitions include Alderson, UNDATED ("Epidemiological Method"); Amdur, et. al., 1991 (*Casarett and Doull's Toxicology*); ATSDR, UNDATED (*Toxicological Profile Glossary)*; EPA, 1986a ("Guidelines for Estimating Exposures"); EPA, 1986b (*EPA Toxicology Handbook*); EPA, 1988a ("Part II. Proposed Guidelines for Assessing Female Reproductive Risk"); EPA, 1988b ("Part III. Proposed Guidelines for Assessing Male Reproductive Risk"); EPA, 1991b ("Guidelines for Developmental Toxicity Risk Assessment"); EPA, 1994e (HEAST); EPA, 1995d (IRIS® glossary); Hodgson, et. al., 1988 (*Dictionary of Toxicology)*; Huntsberger and Leaverton, 1970 (*Statistical Inference in Biomedical Sciences*); Lilienfeld and Lilienfeld, 1988 (*Foundations of Epidemiology)*; Norell, 1992 (*A Short Course in Epidemiology)*; and Dorland, 1994 (*Dorland's Illustrated Medical Dictionary*).

Acute Toxicity: Immediate toxicity. Its former use was associated with toxic effects that were severe (e.g., mortality) in contrast to the term "subacute toxicity" that was associated with toxic effects that were less severe. The term "acute toxicity" is often confused with that of acute exposure.

Association: In a formal, scientific context, a statistical relationship between a disease or adverse effect and biological or social characteristics.

Carcinogenicity: The ability of an agent to induce a cancer response.

Chronic Toxicity: Delayed toxicity. However, the term "chronic toxicity" also refers to effects that persist over a long period of time whether or not they occur immediately or are delayed. The term "chronic toxicity" is often confused with that of chronic exposure.

Confounder (Confounding Variable, Factor): A factor that is covariant with the studied exposure in the study base and masks the ability to distinguish the risk of developing the studied disease occasioned by any association between exposure and disease.

Developmental Toxicity: Adverse effects produced prior to conception, during pregnancy, and 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.

Dose-Response: The relationship between the amount of an agent (either administered, absorbed, or believed to be effective) and changes in certain aspects of the biological system (usually adverse effects), apparently in response to that agent.

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.

Extrapolation: An estimation of a numerical value of an empirical (measured) function at a point outside the range of data which were used to calibrate the function. For example, the quantitative risk estimates for carcinogens (according to EPA guidelines at the time of this writing) are generally low-dose extrapolations based on observations made at higher doses. Another example is extrapolation of health effects from occupational to general exposure levels.

Human Equivalent Concentration (HEC): The human exposure concentration of an agent that is believed to induce the same magnitude of toxic effect as that which a known animal or occupational exposure concentration has induced. For HEC, the exposure concentration has been adjusted for dosimetric differences between experimental animal species and humans. If occupational human exposures are used for extrapolation, the human equivalent concentration represents the equivalent human exposure concentration adjusted to a continuous basis.

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.

Irritation: An inflammatory response, usually of skin, eye, or respiratory tract, induced by direct action of an agent.

LC_{50} (Lethal Concentration): The concentration of a chemical in air that causes death in 50 percent of the test organisms at the end of the specified exposure period. LC_{50} values typically represent acute exposure periods, usually 48 or 96 hours. Typical units are mg/m^3 or ppm.

LD_{50} (Lethal Dose): The dose of a chemical taken by mouth, absorbed by the skin, or injected that is estimated to cause death in 50 percent of the test animals.

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.

Modifying Factor (MF): An uncertainty factor that is greater than zero and less than or equal to 10; the magnitude of the MF depends upon the professional assessment of scientific uncertainties of the study and data base not explicitly treated with the standard uncertainty factors (e.g., the completeness of the overall data base and the number of species tested); the default MF is 1.

Mutagen: An agent that produces a permanent genetic change in a cell (other than changes that occur during normal genetic recombination).

Neurotoxicity: Any toxic effect on any aspect of the central or peripheral nervous system. Such changes can be expressed as functional changes (such as behavioral or neurological abnormalities) or as neurochemical, biochemical, physiological or morphological perturbations.

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.

Odds Ratio (OR): A technique for estimating the relative risk (see below) from case-control (retrospective) studies. This refers to the odds, among diseased individuals, of being exposed as compared to non-diseased individuals.

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

Proportionate Mortality Ratio (PMR): The number of deaths from a specific cause and in a specific period of time per 100 deaths in the same time period.

q_1^*: See Slope Factor.

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.

Reportable Quantity (RQ): The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Reportable quantities are: (1) one pound; or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity: The occurrence of effects on the male or female reproductive system that may result from exposure to environmental agents. The manifestations of such toxicity may include alteration in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of the reproductive system.

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.

Risk Assessment: The determination of the kind and degree of hazard posed by an agent, the extent to which a particular group of people has been or may be exposed to the agent, and the present or potential health risk that exists due to the agent.

Risk Characterization: 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.

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 $(mg/kg\text{-}day)^{-1}$.

Standardized Mortality Ratio (SMR): The ratio of observed events to events expected if the age- and sex-specific mortality rates of a standard population (usually the general population) are applied to the population under study.

Structure Activity Relationship (SAR): The relationship of the molecular structure and/or functional groups of a chemical with specific effects. SARs evaluate the molecular structure of a chemical and make qualitative or quantitative correlations of particular molecular structures and/or functional groups with specific effects.

Subchronic Exposure: Multiple or continuous exposures occurring usually over 3 months. This applies to animal, not human, exposure.

Subchronic Toxicity: Effects from subchronic exposure. This also applies to animal, not human exposure.

Uncertainty Factor (UF): One of several, generally 10-fold factors, used in operationally deriving the RfD or RfC from experimental data. UFs are intended to account for: (1) the variation in sensitivity among the members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure; and (4) the uncertainty in using LOAEL data rather than NOAEL data.

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).

Upper Bound: An estimate of the plausible upper limit to the true value of the quantity. This is usually not a statistical confidence limit unless identified as such explicitly, together with a confidence level.

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.)

ADDITIONAL TERMS: The following additional terms are not used in this module discussion *per se*, but are likely to be found in the literature pertaining to human health hazard and toxicity studies.

Acute Exposure: Exposure occurring over a short period of time. (The specific time period varies depending on the test method and test organism or the receptor of interest.)

Case-Control Study: An epidemiological study in which comparisons are made between a group of persons who have a disease (cases) and a group who do not (controls) regarding possible exposures prior to study.

Case Report: An anecdotal description of the occurrence of a disease or adverse effect in an individual or group of individuals.

Case Study: A detailed analysis of an individual or group.

Chronic Exposure: Continuous or intermittent exposure occurring over an extended period of time, or a significant fraction of the animal's or the individual's lifetime.

Cohort Study: Epidemiological study comparing the morbidity and/or mortality of a group or groups of people (called exposed) who have had a common insult (e.g., exposure to a chemical suspected of causing disease) with a group believed to be unexposed or with the general population.

Correlation: The degree to which two or more phenomena occur together or vary in similar directions.

Cross-Sectional Study: An epidemiological study in which comparisons are made between a group of persons who are found to have an exposure and a group who does not (unexposed). The characteristics under comparison are present in both exposed and unexposed groups at the time of the study and exposure status is often determined after individuals are selected for study. Also called a "prevalence" study.

EPA Health Advisory: An estimate of acceptable drinking water levels for a chemical, based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Human Equivalent Concentration (HEC): See definition for Human Equivalent Dose.

Human Equivalent Dose (HED): The human dose of an agent that is believed to induce the same magnitude of toxic effect as that which a known animal or occupational dose has induced. For HEC, the dose has been adjusted for dosimetric differences between experimental animal species and humans. If occupational human exposures are used for extrapolation, the HED represents the equivalent human exposure concentration adjusted to a continuous basis.

Irreversible Effect: Effect characterized by the inability of the body to partially or fully repair injury caused by a toxic agent.

Latency Period: The time between the initial induction of a health effect and the manifestation (or detection) of the health effect; crudely estimated as the time (or some fraction of the time) from first exposure to detection of the effect.

Potentiation: The ability of one chemical to increase the effect of another.

Prevalence Study: An epidemiological study that examines the relationship between exposure and diseases as they exist at a given period in time. (See also Cross-Sectional Study.)

Prospective Study: A study using a population sample based on exposure status, where exposure may be related to the development of the disease under investigation. The individuals are then followed for several years to see which ones develop and/or die from the disease. Also described by the terms "cohort," "incidence," and "longitudinal." When based on exposure status determined from some time in the past, this may be called "historical prospective."

Relative Risk: The likelihood that an exposed individual will have a disease expressed as a multiple of the likelihood among unexposed (with disease incidence expressed as incidence rate or cumulative incidence).

Retrospective Study: Epidemiological study in which comparisons are made between a group of persons who have a disease (cases) and a group who do not (controls). An attempt is made to determine whether the characteristics (e.g., exposure to a chemical) were present in the past. Also described as "case control," or "case history" studies.

Reversible Effect: An effect that is not permanent, particularly an adverse effect that diminishes when exposure to a toxic chemical ceases.

Spurious Association: A statistical association that represents a statistical artifact or bias. It may arise from biased methods of selecting cases and controls, recording observations or by obtaining information by interview, and cannot be identified with certainty.

Statistical Tests of Significance: Methods for determining on a probabilistic basis if differences in groups under treatment (or observation) could have resulted by chance, or if they represent "rare" events. Also called "statistical tests of hypotheses." The question of random occurrence may be put in the form of a hypothesis to be tested, called the "null hypothesis."

Subacute Exposure: A term, no longer commonly used, that denotes exposures that are longer than acute and shorter than subchronic.

Subacute Toxicity: Effects from subacute exposure.

Subclinical Toxicity: An observable effect which may or may not have any clinical significance (i.e., not biologically significant). With humans it may also mean that the individual's illness is undetected.

Toxicity Assessment: Characterization of the toxicological properties and effects of a chemical, including all aspects of its absorption, metabolism, excretion and mechanism of action, with special emphasis on the identification of a dose-response relationship.

Transient Effect: An effect that disappears over time (irrespective of whether or not exposure continues).

APPROACH/METHODOLOGY: The following presents a summary of the technical approach or methodology for preparing a summary human health hazards profile for a CTSA. Further details for Steps 4 through 8 are presented in the next section of this module.

Step 1: Obtain the CAS RN, synonyms, and information on the chemical structure from the Chemical Properties module.

Step 2: Review the Environmental Fate Summary module to determine if the chemical persists long enough in any environmental medium to be a potential health hazard and if any chemical degradation products need to be considered.

Step 3: Review preliminary exposure pathways from the Exposure Assessment module, if available. The main routes to consider are oral, inhalation, and dermal.

Step 4: Obtain peer-reviewed literature, beginning with secondary sources (e.g., EPA's Integrated Risk Information System [IRIS], EPA review documents, Agency for Toxic Substance and Disease Registry [ATSDR] Profiles, and the Hazardous Substances Data Bank [HSDB]). Resort to primary sources (e.g., journal articles) only when secondary sources are lacking or when more recent information is available in the primary literature that adds new information to the data base for that chemical.

This should include a review of the pharmacokinetics of the chemical and an evaluation of the following toxicological endpoints for both humans and animals:

- Acute toxicity.
- Irritation/sensitization.
- Neurotoxicity.
- Subchronic/chronic toxicity (includes systems such as renal, hepatic, hematopoietic, etc.).
- Developmental/reproductive toxicity.
- Genotoxicity.
- Carcinogenicity.

Step 5: Review the acquired literature and critically evaluate the quality of studies (e.g., use of controls, appropriate numbers of animals, selection of appropriate human study groups, statistical analysis of the data).

Step 6: Construct a health hazards profile for each chemical using the most recent data available. Measured data should take precedence over modeled data. Toxicity summaries should include NOAELs, LOAELs, and RfDs or RfCs for chemicals not causing cancer; and q_1*, unit risk values, and weight-of-evidence classifications for carcinogens. Secondary sources that may contain these types of data are listed in Table 5-11: Sources of Human Health Hazard Data.

Note: Data requirements for toxicity summaries may change as EPA guidance is updated, e.g., changes in the proposed carcinogen risk assessment guidelines (EPA, 1996b).

Present the data clearly and accurately, using consistent units so that comparisons may be easily made. Use the original dose units as well as converted units where possible. Note any assumptions made in dose conversions. Explicitly identify any data that are not peer-reviewed.

Step 7: If some chemicals do not have the values listed in Step 6 and if the necessary data are available, RfDs, carcinogenicity slope factors, and unit risk values or other measures may be calculated. See Details: Step 7 (below), and Table 5-10: Published Guidance on Health Hazards Assessment.

Step 8: In a tabular format, list the toxicity values and classifications that are described in Step 6 (see Details: Step 8, below) and provide to the Risk Characterization module.

METHODOLOGY DETAILS: This section presents methodology details for completing Steps 4 through 8. If necessary, additional information on these and other steps can be found in the previously published guidance (see Table 5-10: Published Guidance on Health Hazards Assessment).

Details: Step 4, Obtaining Literature Information

In vitro studies are useful for mutagenicity assays and for determining structure-activity relationships and mechanisms of toxicity. Note that because of the importance of the various manifestations of neurotoxicity, EPA places these effects in a separate section, rather than under acute or chronic/subchronic toxicity, which could also be appropriate.

Toxicity values that are important for risk characterization include, but are not limited to, the following:

- LD_{50} values for mammalian species.
- Concentrations of the chemical that cause irritation to the eyes, nose, or respiratory passages.
- Concentrations or doses that result in acute neurotoxicity; NOAEL and/or LOAEL for subchronic/chronic neurotoxicity.

- NOAEL and/or LOAEL for subchronic/chronic non-carcinogenic systemic effects. If an RfD is available, inclusion of the experimental details of the key study used to derive that value is required.
- NOAEL or LOAEL for developmental/reproductive toxicity. Note that RfDs may be based on developmental or reproductive effects.
- Epidemiological or animal bioassay data for carcinogenicity. This would include q_1* and unit risk values, if available. The EPA, National Toxicology Program, and IARC classify chemicals as to their carcinogenicity. These classifications should be included when available. (Note that epidemiological data may be available for other adverse effects such as developmental or reproductive effects.)
- Regulatory standards and guidelines (e.g., RfDs and RfCs; Occupational Safety and Health Administration [OSHA], American Conference of Governmental Industrial Hygienists, Inc. [ACGIH], and National Institute for Occupational Safety and Health [NIOSH] exposure limits; drinking water standards; and drinking water health advisories).

Details: Step 5, Evaluating Data Quality

Statistics are used to evaluate the magnitude of response in a study and to determine if an effect is the result of exposure to a chemical. If statistics have not been performed on a particular study, and if there are data for more than one dose, one possible protocol would be to first test for a trend. If there is no trend, then determine if any dose group shows an increase or decrease relative to controls. If data are quantal proportions, some form of categorical analysis is appropriate.

Commonly used statistical tests include analysis of variance and Bartlett's tests for homogeneity (for endpoints such as organ and body weights, hematology, and biochemistry); Dunnett's multiple comparison tables (for significance of differences); and life table test, incidental tumor test, Fisher's exact test, and Cochran-Armitage trend test (for analysis of tumor incidence data). Statistical methods are described in references listed in Table 5-10. A statistician and a health hazard assessment expert should be consulted for information regarding when and how these tests are used and whether they are appropriate for the data in hand. It is generally not necessary to perform statistics on data from HSDB, NIOSH, ATSDR, IRIS or other references listed under Sources of Human Health Hazards Data in Table 5-11.

Details: Step 6, Constructing the Health Hazards Profile

The level of detail presented in the health hazards profile may vary. For example, key studies (such as those used in the derivation of toxicity values such as chronic RfDs, RQs, or carcinogenicity slope factors) require more detailed reporting than supporting studies. A detailed, but concise, description would include experimental details and incidence data for effects, relating exposure and effect. Supporting studies may be described with fewer details and, where appropriate, as ranges of values. Adequate citations should be provided for both key and supporting studies. When epidemiological data are available, epidemiological summaries

should include population observed, comparison population, SMRs, PMRs, or ORs and confounding factors.

The health hazards profile for discrete organic chemicals can be constructed using concentrations or doses derived from experimental studies or can be estimated from structure activity relationships (SARs; see next paragraph). The toxicity of inorganic chemicals typically cannot be accurately estimated using SARs. The hazard profile for inorganic chemicals should therefore be constructed using effective concentrations based on measured toxicity test data. If no data are available, actual data from the nearest structural analog can be used. Chemical mixtures such as petroleum products (i.e., mineral spirits or solvent naphtha) may be evaluated from information on the mixture, information from a "sufficiently similar" mixture, or information on the individual components of the mixture. Constructing a Health Hazard Profile for chemical mixtures is a complex process and the EPA "Guidelines for the Health Risk Assessment of Chemical Mixtures" should be consulted (see published guidance listed in Table 5-10).

When measured data are not available, evaluate data from studies on structurally-related compounds. The use, application, development, and validation of SARs have been discussed in a number of publications (see *Federal Register* citations in Table 5-10). The use and interpretation of SARs require expertise and caution. Computer models that calculate toxicity values based on SARs are available (see Table 5-9: Computer Programs Used in Human Health Hazards Assessment). Briefly, the EPA approach to SARs involves the evaluation and interpretation of available and pertinent data on the chemical under study or its potential metabolites; evaluation of test data on analogous substances and potential metabolites; and the use of mathematical expressions for biological activity or quantitative structure activity relationships (QSARs).

Details: Step 7, Deriving Health Hazard Values

Reference Dose/Reference Concentration (RfD/RfC)

RfDs and RfCs are derived following a thorough examination of the toxicologic and epidemiologic literature for the subject chemical and selection of the studies that are judged to be appropriate for risk assessment. The LOAEL or NOAEL (chronic, subchronic, developmental, or reproductive toxicity) is divided by uncertainty factors and a modifying factor to derive the RfD. If a study has more than one NOAEL, the highest is selected. If there is no NOAEL the RfD may be derived from a LOAEL by applying an uncertainty factor of up to 10. The lowest of the LOAELs for systemic, developmental, or reproductive toxicity is chosen.

The RfD is calculated as follows:

$$\text{RfD} = \frac{\text{NOAEL (mg/kg-day)}}{\text{UFs x MF}}$$

where:

NOAEL = No-observed adverse effect level
UFs = Uncertainty factors
MF = Modifying factor (see Definition of Terms)

Ufs account for the following:

- The variation in sensitivity among the members of the human population (a factor of 10).
- The extrapolation of animal data to humans (a factor of 10).
- Extrapolation from less than lifetime exposure (a factor of 10).
- The use of LOAEL, rather than NOAEL, data (a factor of 10).
- Extrapolation from experimental data that do not fully consider all possible adverse effects (a factor of from 1 to 10).

The methodology for the inhalation RfC includes dosimetric adjustments to account for the species-specific relationships of exposure concentrations to deposited/delivered doses. This requires knowledge of the anatomy and physiology of the lungs and airways to accurately estimate the amount of the inhaled chemical that would reach the tissue where the effects occur. The RfC is calculated similarly to RfD, as follows:

$$RfC = \frac{NOAEL_{[HEC]}\ (mg/m^3)}{UFs \times MF}$$

where:

$NOAEL_{[HEC]}$ = the NOAEL or equivalent effect level dosimetrically adjusted to a human equivalent concentration (HEC)

Slope Factor

The slope factor is a measure of the incremental risk or increased likelihood of an individual developing cancer if exposed to a unit dose of the chemical for a lifetime. The risk is expressed as a probability (i.e., one chance in ten or one chance in one million), and the unit dose is normally expressed as 1 mg of the chemical per unit body weight (kg) per day:

Slope Factor = Risk per unit dose, or Risk per mg/kg-day

When based on animal data, the slope factor is derived by extrapolating from the incidences of tumors occurring in animals receiving high doses of the chemical to low exposure levels expected for human contact in the environment. The EPA uses q_1* for its risk assessments (see definition of slope factor). The q_1* for a chemical, in units of $(mg/kg\text{-}day)^{-1}$, is based on the linearized multistage procedure for carcinogenesis and can be calculated by computer program (e.g., GLOBAL).

Slope factor or q_1* values are used in the Risk Characterization module to estimate cancer risk (in the range where it is expected to be linearly related to exposure). It should be noted that the

proposed carcinogen risk assessment guidelines (EPA, 1996b), if adopted, may require modifications to this approach.

Unit Risk

The slope factor, or q_1*, can also be used to determine the incremental cancer risk that would occur if the chemical was present in an environmental medium such as drinking water at a unit concentration (i.e., 1 μg of chemical per liter of drinking water). The calculation for drinking water usually assumes the person weighs 70 kg and drinks 2 liters of water per day:

$$\text{Drinking Water Unit Risk} = q_1^* \times 1/70 \text{ kg} \times 2 \text{ L/day} \times 10^{-3}$$

Air unit risk (risk per µg/m^3) is derived from the linearized multistage procedure and calculated using the GLOBAL program.

Details: Step 8, Tabulating Toxicity Values

Table 5-8 is an example format for tabulating toxicity values.

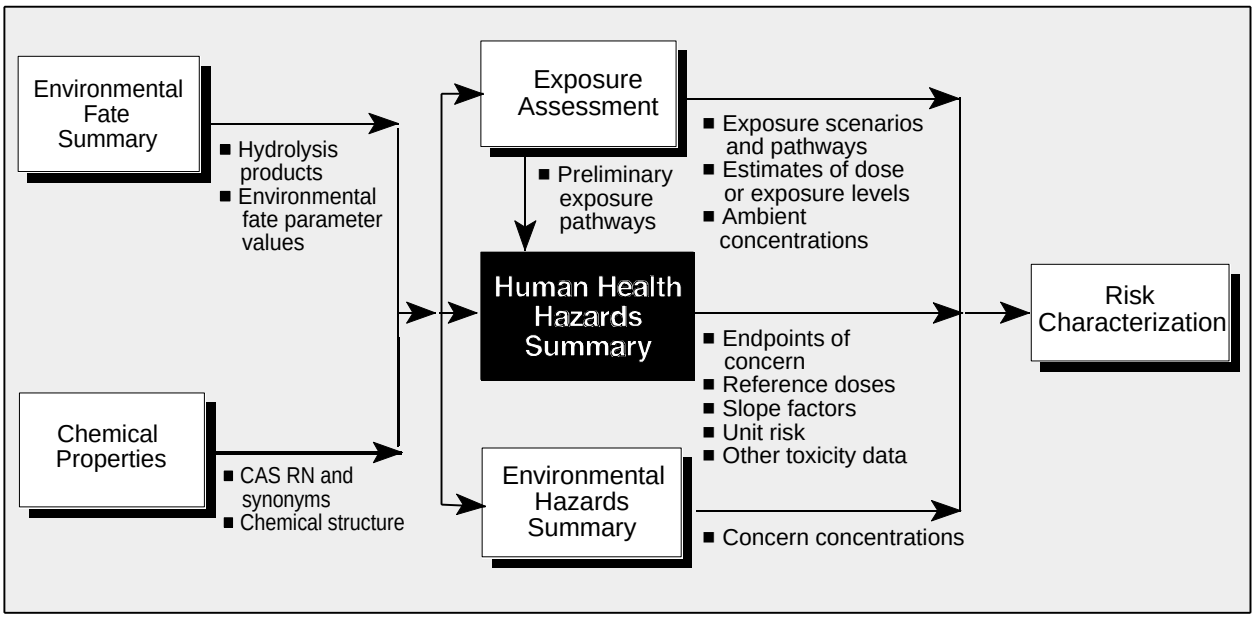
TABLE 5-8: SUMMARY TABLE FOR TOXICITY OF CHEMICALS AND POTENTIAL SUBSTITUTES

Chemical	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10
LD_{50}/LC_{50}										
Irritation (yes or no)										
1. eye	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
2. skin	2.	2.	2.	2.	2.	2.	2.	2.	2.	2.
3. respiratory	3.	3.	3.	3.	3.	3.	3.	3.	3.	3.
Sensitization (yes or no)										
Neurotoxicity (yes or no)										
Developmental Toxicity (yes or no)										
NOAEL/LOAEL[a] (target organ or effect)										
RfD/RfC										
EPA WOE[b]										
Oral Slope Factor $(mg/kg\text{-}day)^{-1}$										
Unit Risk										
1. air (risk per µg/m^3)	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
2. water (risk per µg/L)	2.	2.	2.	2.	2.	2.	2.	2.	2.	2.
Exposure Limits										
1. ACGIH	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
2. OSHA	2.	2.	2.	2.	2.	2.	2.	2.	2.	2.
3. NIOSH	3.	3.	3.	3.	3.	3.	3.	3.	3.	3.

a) If more than one NOAEL select the highest; if no NOAEL, but more than one LOAEL, select the lowest. Include NOAEL/LOAELs for neurotoxicity and developmental toxicity, if available.
b) WOE = weight-of-evidence classification for carcinogenicity.

FLOW OF INFORMATION: This module receives information from the Chemical Properties, Environmental Fate Summary, and Exposure Assessment modules, and transfers information to the Risk Characterization module. Example information flows are shown in Figure 5-5. This module can also be used alone to guide the selection and use of chemicals that are less toxic to humans.

FIGURE 5-5: HUMAN HEALTH HAZARDS SUMMARY MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: Table 5-9 presents references of computer programs that can be used when estimating toxicity reference values.

TABLE 5-9: COMPUTER PROGRAMS USED IN HUMAN HEALTH HAZARDS ASSESSMENT

Reference	Type of Model
GLOBAL92 ICF Kaiser International, Inc.	A program which uses quantal cancer dose-response animal bioassay data to predict the probability of a specific health effect by fitting a specific form of mathematical model to the data provided.

TABLE 5-9: COMPUTER PROGRAMS USED IN HUMAN HEALTH HAZARDS ASSESSMENT	
Reference	**Type of Model**
QSAR: A Structure-Activity Based Chemical Modeling and Information System. 1986.	Modified structure-activity correlations are used to estimate chemical properties, behavior, and toxicity. Developed by U.S. EPA, Environmental Research Laboratory, Duluth, MN, Montana State University Center for Data Systems and Analysis, and Pomona College Medicinal Chemistry Project.
RISK81 Contact Daniel Krewski Health and Welfare Canada	For low-dose extrapolation of quantal response toxicity data.
TOXRISK Crump, K., et. al. 1995.	Software package for performing standard types of health risk assessments. Provides some quantal and time-to-tumor models.

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

PUBLISHED GUIDANCE: Table 5-10 presents references for published guidance on health hazard assessment.

TABLE 5-10: PUBLISHED GUIDANCE ON HEALTH HAZARDS ASSESSMENT	
Reference	**Type of Guidance**
Abramson, J.H. 1988. *Making Sense of Data: A Self-Instruction Manual*.	Interpretation of epidemiological data.
Armitage, P. and G. Berry. 1994. *Statistical Methods in Medical Research*.	Methods for statistical analysis.
Barnes, D.G. and M. Dourson. 1988. "Reference Dose (RfD): Description and Use in Health Risk Assessments."	Condensed description of RfD derivation.
Breslow, N.E. and N.E. Day. 1980. *Statistical Methods in Cancer Research. Vol. I: The Analysis of Case-control Studies*.	Methods for the statistical analysis of epidemiological studies.
Breslow, N.E. and N.E. Day. 1987. *Statistical Methods in Cancer Research. Vol. II: The Analysis of Cohort Studies*.	Methods for the statistical modeling of epidemiological studies.
Clayton, D. and M. Hills. 1993. *Statistical Models in Epidemiology*.	Methods for the statistical modeling of epidemiological studies.

TABLE 5-10: PUBLISHED GUIDANCE ON HEALTH HAZARDS ASSESSMENT

Reference	Type of Guidance
Gad, S.D. and C.S. Weil, Eds. 1986. *Statistics and Experimental Design for Toxicologists*.	Methods for statistical analysis.
Gart, J.J., et. al. 1986. *Statistical Methods in Cancer Research. Vol. III: The Analysis of Long-term Animal Experiments.*	Methods for the statistical analysis of chronic animal studies.
O'Bryan, T.R. and R.H. Ross. 1988. "Chemical Scoring System for Hazard and Exposure Identification."	Ranking system for 11 parameters, including acute and chronic toxicity.
Snedecor, G.W. and W.G. Cochran. 1980. *Statistical Methods*.	General statistical methods.
U.S. Environmental Protection Agency. 1984a. *Methodology and Guidelines for Ranking Chemicals Based on Chronic Toxicity Data*.	Describes derivation of reportable quantity (RQ); incorporates a 10-point severity ranking system for the chronic toxicity of chemicals that can be used in risk characterization.
U.S. Environmental Protection Agency. 1985. *Toxic Substances Control Act Test Guidelines: Final Rules*.	Describes guidelines for performing tests of chemical fate and environmental and health effects.
U.S. Environmental Protection Agency. 1986c. "Guidelines for Carcinogen Risk Assessment."	Describes procedure for the performance of risk assessment on potential chemical carcinogens. (Soon to be revised.)
U.S. Environmental Protection Agency. 1986d. "Guidelines for Mutagenicity Risk Assessment."	Describes procedure for the performance of risk assessment on potential chemical mutagens.
U.S. Environmental Protection Agency. 1986e. "Guidelines for the Health Risk Assessment of Chemical Mixtures."	Describes procedure for the performance of risk assessment on mixtures of chemicals.
U.S. Environmental Protection Agency. 1988a. "Part II. Proposed Guidelines for Assessing Female Reproductive Risk and Request for Comments."	Proposed guidelines for the evaluation of potential toxicity of environmental agents to the human female reproductive system. Provides discussion of female reproductive organs and their functions, endpoints of toxicity in animal assays, human studies, and risk assessment.
U.S. Environmental Protection Agency. 1988b. "Part III. Proposed Guidelines for Assessing Male Reproductive Risk and Request for Comments."	Proposed guidelines for the evaluation of potential toxicity of environmental agents to the human male reproductive system. Provides discussion of male reproductive organs and their functions, endpoints of toxicity in animal assays, human studies, and risk assessment.

TABLE 5-10: PUBLISHED GUIDANCE ON HEALTH HAZARDS ASSESSMENT	
Reference	**Type of Guidance**
U.S. Environmental Protection Agency. 1989a. *Risk Assessment Guidance for Superfund. Volume I. Human Health Evaluation Manual (Part A).*	Guidance for developing human health risk assessments at Superfund sites.
U.S. Environmental Protection Agency. 1991b. "Guidelines for Developmental Toxicity Risk Assessment."	Discusses basics of developmental toxicity and EPA's risk assessment process for developmental toxins.
U.S. Environmental Protection Agency. 1991c. *General Quantitative Risk Assessment Guidelines for Noncancer Health Effects*.	Discusses various aspects of risk assessment (hazard identification, dose-response assessment, risk characterization). A draft document to be used as guidance; not necessarily Agency policy at present.
U.S. Environmental Protection Agency. 1992a. "Guidelines for Exposure Assessment."	Provides a general approach and framework for carrying out human or nonhuman exposure assessments for specified pollutants. To be used for risk assessment in conjunction with toxicity/effects assessment.
U.S. Environmental Protection Agency. 1993b. "Draft Report: Principles of Neurotoxicity Risk Assessment."	Discusses basics of neurotoxicity and EPA's risk assessment process for neurotoxins. A draft document to be used as guidance; not necessarily Agency policy at present.
U.S. Environmental Protection Agency. 1994f. *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*.	Describes procedure for the derivation of an inhalation reference dose.

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

DATA SOURCES: Table 5-11 lists sources of health hazard data that should be readily available to most hazard assessors.

TABLE 5-11: SOURCES OF HUMAN HEALTH HAZARDS DATA	
Reference	**Type of Data**
Clayton, G.D. and F.E. Clayton. 1994. *Patty's Industrial Hygiene and Toxicology*.	Toxicology and properties of selected industrial chemicals and classes of chemicals.
Documentation of the Threshold Limit Values and Biological Exposure Indices. UNDATED.	Review of toxicity and rationale for selection of ACGIH exposure levels.

TABLE 5-11: SOURCES OF HUMAN HEALTH HAZARDS DATA

Reference	Type of Data
HSDB®. Hazardous Substances Data Bank (HSDB). Updated Periodically.	An on-line data base that contains information on a chemical's properties, human and environmental toxicity, environmental fate, regulations, and treatments.
International Agency for Research on Cancer (IARC). 1979. *IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man*.	Reviews the carcinogenicity of chemicals. Provides IARC classification.
International Agency for Research on Cancer (IARC). 1987. *IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Overall Evaluations of Carcinogenicity*.	Summary of IARC Monographs, Volumes 1 to 42. Contains rationale for IARC weight-of- evidence classifications.
International Programme on Chemical Safety (IPCS). UNDATED. *Environmental Health Criteria Documents*.	A series of chemical profiles that include information on exposure and toxicity.
National Institute for Occupational Safety and Health (NIOSH). UNDATEDa. *Health Effects Documents*.	Literature review of occupational exposure data, health effects data, and animal studies. Rationale for the derivation of NIOSH exposure levels.
National Institute for Occupational Safety and Health (NIOSH). 1992. *NIOSH Recommendations for Occupational Safety and Health. Compendium of Policy Documents and Statements*.	NIOSH occupational exposure limits.
National Toxicology Program (NTP). UNDATED. *NTP Toxicology and Carcinogenesis Studies*.	Reports results of NTP bioassays for carcinogenicity and chronic toxicity. Provides NTP classification.
U.S. Air Force. 1989. *The Installation Restoration Toxicology Guide, Vols. 1-5*.	Toxicological profiles of hazardous chemicals found at U.S. Air Force sites. In addition to health effects, these documents review properties, regulations, and exposure.
U.S. Department of Health and Human Services. UNDATEDa. *Toxicological Profiles*.	Toxicological profiles of hazardous chemicals most often found at facilities on CERCLA's National Priority List. In addition to health effects and risk levels, these documents review properties, regulations, and exposure.
U.S. Department of Labor, Occupational Safety and Health Administration. 1989a. "Table Z-2. Limits for Air Contaminants."	OSHA occupational exposure limits.

TABLE 5-11: SOURCES OF HUMAN HEALTH HAZARDS DATA	
Reference	**Type of Data**
U.S. Environmental Protection Agency. UNDATEDa. *Drinking Water Regulations and Health Advisories*.	Maximum Contaminant Levels for drinking water (MCLs), Maximum Contaminant Level Goal (MCLGs), drinking water health advisories, and ambient water quality criteria for the protection of human health. MCLs are promulgated pursuant to the Safe Drinking Water Act. MCLG is a non-enforceable concentration of a drinking water contaminant that is protective of adverse human health effects and allows an adequate margin of safety.
U.S. Environmental Protection Agency. UNDATEDb. *Health Assessment Documents (HAD)*.	Reviews of health effects of specific chemicals.
U.S. Environmental Protection Agency. UNDATEDc. *Integrated Risk Information System (IRIS®)*.	Agency position on selected substances, including reviews of selected studies used in the derivation of RfD, RfC, q_1*, and unit risk values. When appropriate data are available, provides EPA classification of carcinogenicity.
U.S. Environmental Protection Agency. 1991d. *Table 302.4. List of Hazardous Substances and Reportable Quantities.*	RQ values for selected hazardous chemicals.

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

The following data bases (Table 5-12) are useful in the absence of other data, but information given should be checked against primary sources for accuracy. The TOXLINE and TOXLIT sources provide abstracts that sometimes contain useful data; most of these data bases are good sources of references to primary literature, such as journal articles.

TABLE 5-12: SUPPLEMENTAL SOURCES OF HUMAN HEALTH HAZARDS DATA	
Reference	**Types of Data**
CANCERLIT®. 1995.	Bibliographic on-line data base containing information on various aspects of cancer.
CCRIS®. Chemical Carcinogenesis Research Information System. 1995.	Factual data bank sponsored by National Cancer Institute. Contains evaluated data and information, derived from both short- and long-term bioassays on 1,200 chemicals.

TABLE 5-12: SUPPLEMENTAL SOURCES OF HUMAN HEALTH HAZARDS DATA

Reference	Types of Data
CHEMID®. Chemical Identification System. 1995.	A chemical dictionary file for over 184,000 compounds of regulatory and biomedical interest. Includes CAS RNs, molecular formulae, generic and trivial names, MeSH headings, and file locators for other files on the ELHILL® and TOXNET® systems. Also provides names and other data used to describe chemicals on over 20 key federal and state regulatory lists.
CHEMLINE®. Chemical Dictionary Online. 1995.	On-line data base that contains 1,142,000 records. Includes chemical names, synonyms, CAS RNs, molecular formulas, National Library of Medicine file locators and, where appropriate, ring structure information.
DART®. Developmental and Reproductive Toxicology. 1995.	Bibliographic data base covering teratology and developmental toxicology literature published since 1989.
EMICBACK®. Environmental Mutagen Information Center Backfile. 1995.	Contains references to chemical, biological, and physical agents that have been tested for genotoxic activity.
ETICBACK®. Environmental Teratology Information Center Backfile. 1995.	Contains references on agents that may cause birth defects.
GENE-TOX®. Genetic Toxicology. 1995.	An on-line data bank created by the EPA as a multi-phase effort to review and evaluate the existing literature and assay systems available in the field of genetic toxicology.
MEDLINE®. MEDLARS Online. 1995.	Bibliographic data base covering medicine, nursing, dentistry, veterinary medicine, and the preclinical sciences. Good source of epidemiological information.
RTECS®. Registry of Toxic Effects of Chemical Substances. 1995.	On-line data base that briefly summarizes the toxicity of a given chemical (not peer-reviewed).
TOXLINE®. 1995	Bibliographic toxicity data base. Abstracts are available.
TOXLIT®. 1995.	Bibliographic data base. Toxicity files from Chemical Abstracts. Abstracts are available.
U.S. Environmental Protection Agency. UNDATEDd. *Health Effects Assessment Summary Tables*.	RfD, RfC, unit risk, and q_1* values for selected chemicals.

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

ENVIRONMENTAL HAZARDS SUMMARY

OVERVIEW: Environmental hazards assessment is the process of identifying the adverse effects that a chemical may have on organisms in the environment. Currently, the CTSA process for environmental hazards assessment focusses on aquatic toxicity. Other environmental hazards could include mammalian toxicity, avian toxicity, and habitat alteration or destruction (e.g., altering the temperature of a stream by discharging cooling water).

This module collects data on measured or predicted toxicity of chemicals to aquatic organisms to characterize the potential aquatic toxicity hazard of chemical discharges to receiving waters. Toxic chemical discharges can also affect the quality of water that may be a source of drinking water and can be a detriment to the human food chain. Aquatic toxicity data are combined with estimated water concentrations from the Exposure Assessment module to assess the risk of chemical exposure to aquatic organisms in the Risk Characterization module.

GOALS:

- Assess the toxicity of chemicals to the aquatic environment.
- Guide the selection and use of chemicals that are less toxic to aquatic organisms.
- Determine the aquatic toxicity concern concentration (CC) of chemicals.
- Provide the CCs to the Risk Characterization module.

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

- Expertise in aquatic toxicology, including knowledge of standard aquatic toxicity test methods, relative sensitivity of aquatic species to chemical contamination, mechanisms of toxic action, and relationships of the molecular structure of chemicals to toxic action.
- Knowledge of molecular structure and fate of chemicals in the aquatic environment.

Within a business or a DfE project team, the people who might supply these skills include an aquatic toxicologist, an environmental scientist, a chemist, and/or an environmental engineer. DfE project teams that do not have people with the necessary expertise to complete this module should seek outside assistance.

Note: The analysis presented in this module should only be undertaken by someone with expertise in environmental hazards (toxicity) assessment. Furthermore, peer-review of the completed environmental hazards summary is recommended.

DEFINITION OF TERMS:

Analog: A chemical compound structurally similar to another but differing often by a single element of the same valence and group of the periodic table as the element it replaces.

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

Aquatic Toxicity Profile: A compilation of the effective concentrations (EC), either measured or predicted, for a range of species.

Assessment Factor (AsF): Adjustment value used in the calculation of a CC that incorporates the uncertainty associated with: (1) toxicity data (e.g., laboratory test versus field test; measured versus estimated data); (2) acute exposures versus chronic exposures; and (3) species sensitivity.

Chronic Value: (See No Effect Concentration.)

Daphnid: Water flea; an aquatic invertebrate (*Daphnia* spp.) frequently used as the test organism in aquatic toxicity testing.

Effects Concentration (EC_{50}): The concentration of a chemical in water that causes 50 percent of the test organisms to show an adverse sublethal effect (such as growth inhibition) at the end of the specified exposure period. Typical units are mg/L.

Hydrolysis: A chemical transformation process in which a chemical reacts with water. In the process, a new carbon-oxygen bond is formed with oxygen derived from the water molecule, and a bond is cleaved within the chemical between carbon and some functional group.

Lethal Concentration (LC_{50}): The concentration of a chemical in water (or air) that causes death or complete immobilization in 50 percent of the test organisms at the end of the specified exposure period. LC_{50} values typically represent acute exposure periods, usually 48 or 96 hours but up to 14 days for fish. Typical units are mg/L (mg/m^3 or ppm for air).

Lowest-Observed Effect Concentration (LOEC): The lowest concentration at which there are statistically significant increases in adverse effects in the exposed population over its appropriate control group.

Maximum Allowable Toxicant Concentration (MATC): The range of measured values in the range from the no-observed effect concentration (NOEC) to the LOEC.

Measured Concentrations: Chemical concentrations measured in the aqueous test solution at specified intervals and at the end of an aquatic toxicity test period. EPA aquatic toxicity test methods in the Code of Federal Regulations require test results to be reported based on mean measured concentrations. Many tests results are based on nominal concentrations, however, to avoid the cost of chemical laboratory analysis.

No-Effect Concentration (NEC): The concentration of a chemical that results in no significant effects on the test organisms following a prescribed (usually chronic) exposure period. NEC is the geometric mean of the NOEC and the LOEC and is used to represent the threshold concentration. This value may alternatively be called the geometric mean of the maximum allowable toxicant concentration (GMATC), or the Chronic Value. Typical units are mg/L.

No-Observed Effect Concentration (NOEC): A concentration at which there are no statistically significant increases in adverse effects in the exposed population over its appropriate control group.

Nominal Concentrations: Chemical concentrations added to the aqueous test solution at the beginning of an aquatic toxicity test. Nominal concentrations can be higher than the actual concentration causing a toxic effect, particularly if the chemical is volatile or was added to the test solution at a concentration greater than its water solubility limit.

Octanol/Water Partition Coefficient (K_{ow}): The equilibrium ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system, typically expressed in log units (log K_{ow}). K_{ow} provides an indication of a chemical's water solubility, fat solubility (lipophilicity), its tendency to bioconcentrate in aquatic organisms, and to sorb to soil or sediment. It is often used in toxicity structure-activity relationships.

Structure-Activity Relationship (SAR): The relationship of the molecular structure and/or functional groups of a chemical with specific effects. SARs evaluate the molecular structure of a chemical and make qualitative or quantitative correlations of particular molecular structures and/or functional groups with specific effects.

Threshold Concentration: The concentration at which effects begin. (See No Effect Concentration.)

APPROACH/METHODOLOGY: The following presents a summary of the technical approach or methodology for conducting an environmental hazards assessment focussing on aquatic toxicity. Methodology details for Steps 3, 4, 5, and 6 follow this section.

Step 1: Obtain the CAS RN and synonyms, chemical structure, and pertinent chemical properties information for each chemical from the Chemical Properties module.

Step 2: Obtain environmental fate parameter values and reactivity data from the Environmental Fate Summary module. (For example, a chemical's K_{ow} is required to predict effect concentrations.) If a chemical is highly water-reactive (for example, hydrolysis half-life less than one hour) consider collecting toxicity data for the hydrolysis product(s).

Step 3: Construct an aquatic toxicity profile for each chemical. The most frequently used toxicity profile for aquatic organisms consists of the following:

- Fish acute toxicity value (usually a fish 96-hour LC_{50} value).
- Aquatic invertebrate acute toxicity value (usually a daphnid 48-hour LC_{50} value).
- Green algal toxicity value (usually an algal 96-hour EC_{50} value).
- Fish chronic value (usually a fish 28-day early life stage NEC).
- Aquatic invertebrate chronic toxicity value (usually a daphnid 21-day NEC).
- Algal chronic toxicity value (usually an algal 96-hour NEC value for biomass).

Step 4: Use data quality checks to evaluate the validity of the data obtained in Step 3. Data that appear invalid (e.g., based on nominal concentrations instead of measured concentrations; inconsistent with the physical/chemical properties of the chemical, etc.) should be replaced with data of better quality or predicted data.

Step 5: Calculate the CC for each chemical in water. Concentrations in water below the CC are assumed to present low (acceptable) risk to aquatic species.

Step 6: Rank chemicals for aquatic toxicity according to the lowest of their acute or chronic values. This ranking can be based on scoring the chemicals as High, Moderate, or Low concern for aquatic toxicity.

Step 7: Provide the CCs to the Risk Characterization module.

METHODOLOGY DETAILS: This section presents methodology details for completing Steps 3, 4, 5, and 6. If necessary, additional information on this and other steps can be found in previously published guidance (Table 5-15: Published Guidance on Aquatic Toxicity Assessment).

Details: Step 3, Constructing the Aquatic Toxicity Profile

The aquatic toxicity profile may consist of only valid measured data, only predicted values, or a combination of both. Depending on the availability of valid measured data or SARs to estimate data, the toxicity profile may contain a minimum of one acute or chronic value to the full compliment of three acute values and three chronic values. Examples from the Screen Reclamation CTSA (EPA, 1994c) are shown in Table 5-13.

TABLE 5-13: EXAMPLE AQUATIC TOXICITY PROFILES (in mg/L)								
Chemical	**Fish Acute**	**Daphnid Acute**	**Algal Acute**	**Fish Chronic**	**Daphnid Chronic**	**Algal Chronic**	**CC[a]**	**Chronic Eco[b] Hazard Rank**
Acetone	> 1000	> 1000	> 1000	490	100	76	7.6	Low
Sodium hypochlorite	< 1.7	< 2.0	< 2.0	< 0.17	< 0.2	< 0.2	< 0.02	Moderate
Solvent naphtha light aliphatic C^5 - C^{10}	0.64	0.86	0.23	0.05	0.05	0.11	0.005	High

a) CC is derived by dividing the lowest chronic value (in mg/L) by 10.
b) See Details: Step 6 for guidelines on ranking chemicals for aquatic toxicity.

Chemical Mixtures: Chemical mixtures, such as petroleum products (e.g., mineral spirits or solvent naphtha), do not lend themselves to the standard assessment process using SARs. The chemical constituents and the percentage of each in a mixture can vary. The toxicity of mixtures can be determined by estimating the toxicity of each individual constituent and then evaluating the potential toxicity of the product through a weighted average. If the concentration of each constituent in the mixture is not known, one approach is to assume that each component is present in an equal percentage in the product and the geometric mean of the range of like toxicity values provides the best estimate of the toxicity. The geometric mean of *n* positive numbers is $(a \times b \times c...)^{1/n}$. If the concentration of the constituents is known, then the sum of the weight fractions of each constituent multiplied by its toxicity provides an estimate of the toxicity of the product.

Discrete (Single) Organic Chemicals: The toxicity profile for single organic chemicals can be constructed using effective concentrations based on toxicity test data (measured) or estimated toxicity values based on SARs.

Inorganic Chemicals: The toxicity of inorganic chemicals typically cannot be as accurately estimated using SARs as for organic chemicals. The toxicity profile for inorganic chemicals should therefore be constructed using effective concentrations based on measured toxicity test data if possible. If no data are available, actual data from the nearest analog can be used.

To construct the toxicity profile:

(1) Collect valid measured data from peer-reviewed on-line data bases such as Hazardous Substance Data Bank (HSDB) or from peer-reviewed open literature sources.

(2) When valid measured data are not available, use SAR estimates if available for the chemical class. The use, application, development, and validation of SARs have been presented in a number of publications (see section on previously published guidance). Computer models that calculate toxicity values based on SARs are also

available (see section on analytical models). The following data hierarchy is preferred for SAR estimates (from lowest to highest):

a) Valid measured data from the nearest analog.
b) Predicted value based on valid measured data from two analogs that bracket the chemical of concern.
c) Predicted value based on regression equation developed from valid measured data for a similar class of compounds.

Details: Step 4, Evaluating Data Quality

The following are examples of data quality checks. An exhaustive data quality evaluation requires expert judgment and experience.

(1) Determine if the effective concentrations are based on mean measured concentrations or nominal concentrations. Data based on mean measured concentrations are preferred, especially for volatile compounds.

(2) Determine if a chemical's physical/chemical properties are consistent with one another and with the chemical's effective concentrations. For example, a chemical with a low K_{ow} value would be expected to have a high water solubility limit. A chemical's LC_{50} value should be less than or equal to its water solubility limit unless it is a self-dispersing compound such as a surfactant. Measured concentrations that significantly exceed the water solubility limit of a compound suggest that the test laboratory may have artificially enhanced the water solubility to a level that cannot be realized in the environment.

(3) Compare the test methods against the chemical's physical/chemical properties. For example, highly water reactive chemicals (as measured by the hydrolysis half-life) should be tested in a flow-through system instead of a static system where pure stock material is added directly to the system. With the static system the test organism may only be exposed to the hydrolysis products.

Details: Step 5, Calculating the CCs

The CC for each chemical in water is calculated using the general equation:

CC = acute or chronic toxicity value ÷ AsF

AsFs are dependent on the amount and type of toxicity data contained in a toxicity profile and reflect the amount of uncertainty about the potential effects associated with a toxicity value. In general, the more complete the hazard profile and the greater the quality of the toxicity data, the smaller the factor used.

One of the following specific equations is used, depending on the availability of data:

a) If the toxicity profile only contains one or two acute toxicity values (no chronic values):

CC = lowest acute value ÷ 1000

b) If the toxicity profile contains three acute values (no chronic values):

CC = lowest acute value ÷ 100

c) If the toxicity profile contains one chronic value:

CC = chronic value ÷ 10, if the value is for the most sensitive species.

Otherwise:

CC = acute value for the most sensitive species ÷ 100

d) If the toxicity profile contains three chronic values:

CC = lowest chronic value ÷ 10

e) If the toxicity profile contains a measured chronic value from a field study:

CC = measured chronic value ÷ 1

Examples from the Screen Reclamation CTSA (EPA, 1994c) are shown in Table 5-13.

Details: Step 6, Ranking Chemicals for Aquatic Toxicity

Chemicals can be ranked for aquatic toxicity according to the following criteria:

a) For chronic values:

≤ 0.1 mg/L .....High
> 0.1 to ≤ 10 mg/L .....Moderate
> 10 mg/L .....Low

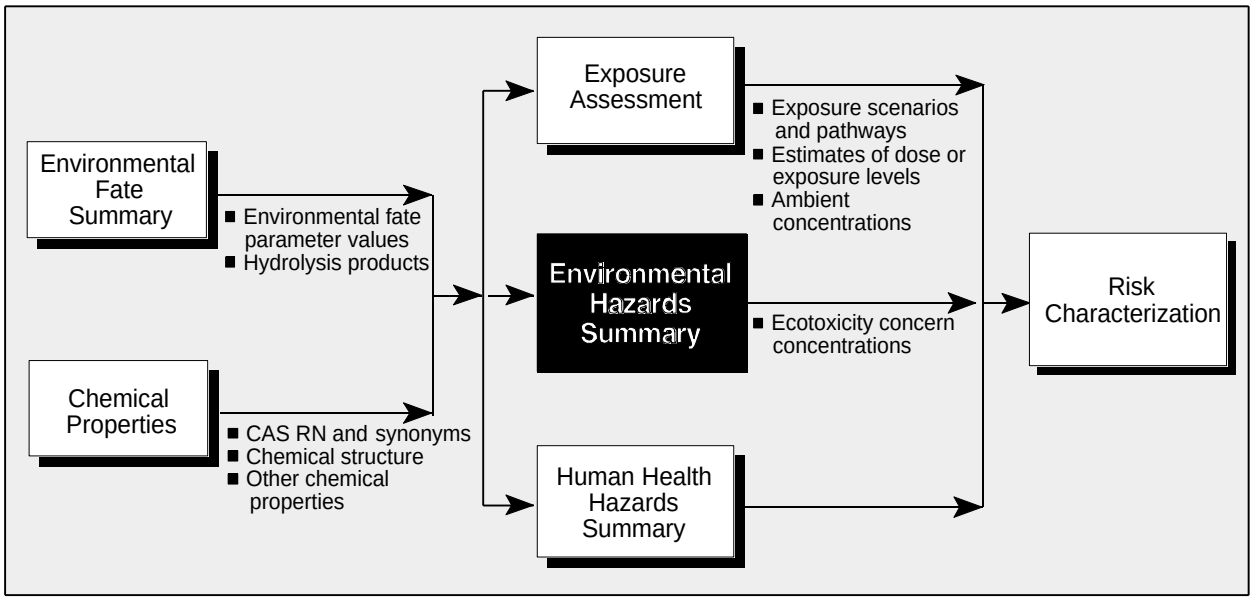
b) For acute values:

≤ 1 mg/L .....High
> 1 to ≤ 100 mg/L .....Moderate
> 100 mg/L .....Low

Chronic toxicity ranking takes precedent over the acute ranking. This relative ranking of toxicity can be used to guide the selection and use of chemicals that are less hazardous to aquatic organisms. Examples from the Screen Reclamation CTSA (EPA, 1994c) are shown in Table 5-13.

FLOW OF INFORMATION: This module can be used alone as a final data point to guide the selection and use of chemicals that are less toxic to aquatic organisms. In a CTSA, this module receives data from the Environmental Fate Summary and Chemical Properties modules and transfers data to the Risk Characterization module. Example information flows are shown in Figure 5-6.

FIGURE 5-6: ENVIRONMENTAL HAZARDS SUMMARY MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: Table 5-14 presents references for SAR models that can be used to predict aquatic toxicity values. Since different SAR models may provide different or conflicting results, one model should be used consistently throughout a particular CTSA project.

TABLE 5-14: ANALYTICAL MODELS USED IN AQUATIC TOXICITY ASSESSMENT

Reference	Type of Model
Clements, R.G. and J.V. Nabholz. 1994. *ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure-Activity Relationships; User's Guide.*	PC format analytical model developed within the constraints of the regulatory program office of Office of Pollution Prevention and Toxics (OPPT). Uses SARs to predict acute and chronic ecotoxicity concentrations for daphnid, fish and algae. EPA uses this system exclusively for evaluating new and existing chemicals.

TABLE 5-14: ANALYTICAL MODELS USED IN AQUATIC TOXICITY ASSESSMENT	
Reference	**Type of Model**
Hunter, R.S. and F.D. Culver. 1992. *MicroQSAR Version 2.0: A Structure-Activity Based Chemical Modeling and Information System*.	Personal computer-based system of models. Uses quantitative SARs to estimate chemical properties and aquatic toxicity values.
QSAR: A Structure-Activity Based Chemical Modeling and Information System. 1986.	Available on-line and in PC format. Uses quantitative SARs to estimate chemical properties, environmental fate parameters, aquatic LC_{50} in 7 common test organisms, and NEC in fathead minnow.

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

PUBLISHED GUIDANCE: Table 5-15 presents references for published guidance on environmental toxicity assessment and the use of SARs.

TABLE 5-15: PUBLISHED GUIDANCE ON AQUATIC TOXICITY ASSESSMENT	
Reference	**Type of Guidance**
Clements, R.G., Ed. 1988. *Estimating Toxicity of Industrial Chemicals to Aquatic Organisms Using Structure Activity Relationships*.	Describes the use of SARs by EPA OPPT.
Clements, R.G., et. al. 1993a. "The Use and Application of QSARs in the Office of Toxic Substances for Ecological Hazard Assessment of New Chemicals."	Describes the use and application of QSARs for the hazard assessment of new chemicals.
Clements, R.G., et. al. 1993b. "The Use of Quantitative Structure-Activity Relationships (QSARs) as Screening Tools in Environmental Assessment."	Describes the development, validation, and application of SARs in EPA OPPT.
Clements, R.G., Ed. 1994. *Estimating Toxicity of Industrial Chemicals to Aquatic Organisms Using Structure-Activity Relationships*.	Describes the use of SARs by EPA OPPT.
Lipnick, R.L. 1993. "Baseline Toxicity QSAR Models: A Means to Assess Mechanism of Toxicity for Aquatic Organisms and Mammals."	Describes the development, validation, and application of SARs in EPA OPPT.
Nabholz, J.V. 1991. "Environmental Hazard and Risk Assessment Under the United States Toxic Substances Control Act."	Detailed discussion of a comprehensive toxicity profile and risk assessment for existing chemicals.

TABLE 5-15: PUBLISHED GUIDANCE ON AQUATIC TOXICITY ASSESSMENT	
Reference	**Type of Guidance**
Nabholz, J.V., et. al. 1993a. "Environmental Risk Assessment of New Chemicals Under the Toxic Substances Control Act (TSCA) Section Five."	Describes the toxicity profile outlined in Step 3.
Nabholz, J.V., et. al. 1993b. "Validation of Structure-Activity Relationships Used by the U.S. EPA's Office of Pollution Prevention and Toxics for the Environmental Hazard Assessment of Industrial Chemicals."	Describes the development, validation, and application of SARs in EPA OPPT.
U.S. Environmental Protection Agency. 1984b. *Estimating Concern Levels for Concentrations of Chemical Substances in the Environment*.	Describes the use of AsFs to determine the CC for a chemical.
Zeeman, M.G. and James Gilford. 1993. "Ecological Hazard Evaluation and Risk Assessment Under EPA's Toxic Substances Control Act (TSCA): An Introduction."	Provides an overview of the process used in the environmental toxicity assessment of chemicals.
Zeeman, M.G., et. al. 1993. "The Development of SAR/QSAR for Use Under EPA's Toxic Substances Control Act (TSCA): An Introduction."	Describes the development, validation, and application of SARs in EPA OPPT.
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 development, validation, and application of SARs in EPA OPPT.

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

DATA SOURCES: Table 5-16 lists sources of aquatic toxicity data.

TABLE 5-16: SOURCES OF AQUATIC TOXICITY DATA	
Reference	**Type of Data**
Aquatic Information Retrieval (AQUIRE) Data Base. UNDATED.	Comprehensive data base of measured aquatic toxicity values derived from open literature. Some data not peer-reviewed. Data should be confirmed with original literature citation.

TABLE 5-16: SOURCES OF AQUATIC TOXICITY DATA

Reference	Type of Data
Brooke, L.T., et. al., Ed. 1984 - 1990. *Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas).*	Comprehensive source of measured fish toxicity values for a single species (fathead minnows), including fish LC_{50} data.
Call, D.J. and D.L. Geiger, Eds. 1992. *Sub-chronic Toxicities of Industrial and Agricultural Chemicals to Fathead Minnows (Pimephales promelas).*	Source of measured fish toxicity values for a single species (fathead minnows), including fish EC_{50} data.
HSDB®. Hazardous Substances Data Bank (HSDB). Updated Periodically.	Measured aquatic toxicity values derived from open literature. Peer-reviewed.
U.S. Atomic Energy Commission. 1973. *Toxicity of Power Plant Chemicals to Aquatic Life*.	Aquatic toxicity values for inorganic chemicals.
U.S. Environmental Protection Agency. UNDATEDe. *Ambient Water Quality Criteria Documents*.	Aquatic toxicity values for chemicals for which ambient water quality criteria have been developed. Useful for organic and inorganic compounds.

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

CHEMISTRY OF USE & PROCESS DESCRIPTION

OVERVIEW: The Chemistry of Use & Process Description module identifies the chemical, physical, and mechanical properties which contribute to the effectiveness of the use cluster chemicals or technologies in an industry- or product-specific application. The module also details the process in which the chemicals are used through the creation of a process flow diagram that schematically describes the process operations, equipment, and material flows.

GOALS:

- Identify the characteristics of a chemical (e.g., low vapor pressure, high solvency, water solubility, ductility, and other chemical, physical, or mechanical chemical properties) that contribute to its effectiveness in achieving the desired function.
- Develop a process flow diagram that describes each operation performed in the application being evaluated.
- Utilize the chemistry of use and process flow diagram to identify potential substitute chemicals, processes, or technologies.
- Provide a basis for developing a survey instrument to evaluate workplace practices in the use cluster industry and to determine the possible sources of chemical release in the use cluster.

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

- Knowledge of basic chemical properties and reactions.
- Ability to create and use process flow diagrams.
- Knowledge of the manufacturing, commercial, or industrial process that is being evaluated.

Within a business or DfE project team, the people who might supply these skills include a chemist, process operator, process supervisor, or a chemical or mechanical engineer. Vendors of any process chemicals or equipment may also be a good resource.

DEFINITION OF TERMS:

Flow Diagram: A block diagram that depicts the equipment, material streams, and basic operations performed in a process.

Material Stream: A flow of material (e.g., water, chemicals, product outputs, air emissions, etc.) either into or out of a step in the process.

Unit Operation: A process step that achieves a desired function.

APPROACH/ METHODOLOGY: The following presents a summary of the approach or methodology for evaluating the chemistry of use and preparing a process description. If there are substantially different methods of performing the use cluster function within an industry, it may be necessary to define the chemistry of use and prepare a process description for each of the methods typically employed. Further methodology details for Step 4 follow this section.

Step 1: Obtain chemical data including CAS RNs, molecular structure, and chemical/physical properties from the Chemical Properties module.

Step 2: Identify the properties that contribute to the effectiveness of the use cluster chemicals or technologies in performing the desired function. The properties may be chemical properties (e.g., a solvent with the ability to dissolve many different types of resins may be required in a paint stripping product), physical properties (e.g., a printing ink may have to be white, thus requiring the ink to contain a white pigment, such as titanium dioxide), or mechanical properties (e.g., a material substrate may need to meet specific mechanical qualifications for yield strength or fracture toughness). These properties are important criteria when selecting alternatives for a particular use cluster and identifying performance characteristics for the Performance Assessment.

Step 3: Examine the industry- or product-specific application of the use cluster chemicals to identify the following:

- Unit Operations, or process steps, required to perform the desired function (e.g., cleaning, degreasing, plating, product assembly, drilling, painting, drying, etc.). Identify any chemical, physical, or mechanical agents used in conjunction with the use cluster chemicals (e.g., dilution with water, heat, pressure, mechanical agitation, etc.).
- Equipment used in the process steps (e.g., production machinery, reactors, heaters, waste stream control technologies, etc.).
- Material streams that flow into, out of, or between steps in the process (e.g., raw material inputs, product outputs, rinse water streams, solid waste disposal, air emissions, waste water discharges, etc.).
- The manner in which raw materials, chemicals, or products are stored and handled (e.g., chemical feedstock handling, methods of storage, etc.).
- Any other data that might be necessary to prepare a process description or process flow diagram.

Step 4: Construct a process flow diagram using the information collected in Step 3. An example flow diagram is shown in the Methodology Details section.

Step 5: Review the information obtained from Steps 1 through 4 with the objective of identifying alternative chemicals, processes, and/or technologies (i.e., substitutes) that could be used to accomplish the same function. One approach to identifying substitutes is to consult with other industries that have similar functional requirements at some stage in the manufacturing or commercial service process. Another approach is to consult with vendors of chemicals or equipment who may be able to suggest process improvements that reduce environmental releases. Also, consult technical assistance organizations that have a broad overview of chemical uses and substitutes in many different industries.

Step 6: Transfer a description of the unit operations and the process flow diagram to the following modules:

- Workplace Practices & Source Release Assessment.
- Process Safety Assessment.
- Exposure Assessment.
- Regulatory Status.
- Pollution Prevention Opportunities Assessment.
- Control Technologies Assessment.
- Performance Assessment.

Step 7: Provide data on material streams (e.g., water, raw materials, chemicals, etc.) to the Resource Conservation module, and a list of equipment used in the process to the Energy Impacts module.

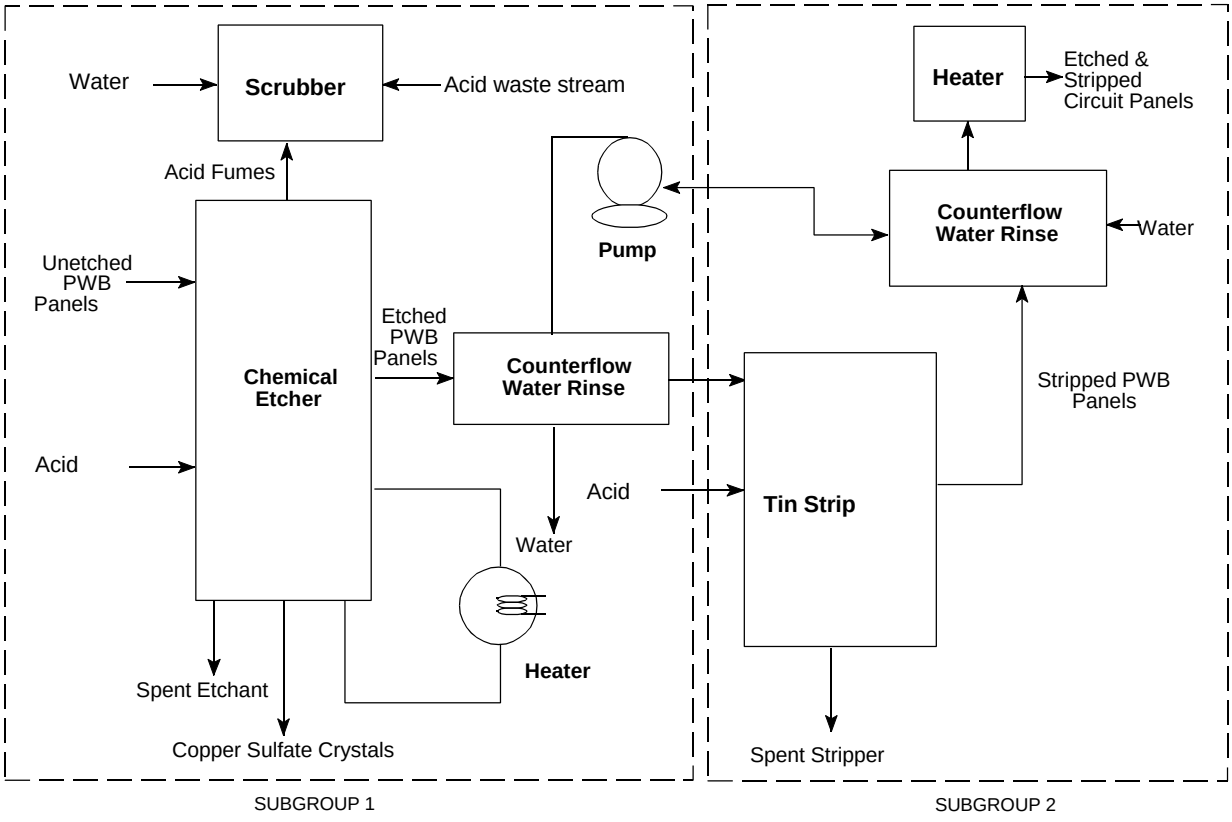
METHODOLOGY DETAILS: This section presents the methodology details for completing Step 4.

Details: Step 4, Process Flow Diagram Example

Figure 5-7 is an example of a process flow diagram for the pattern etching use cluster of the printed wiring board manufacturing process.

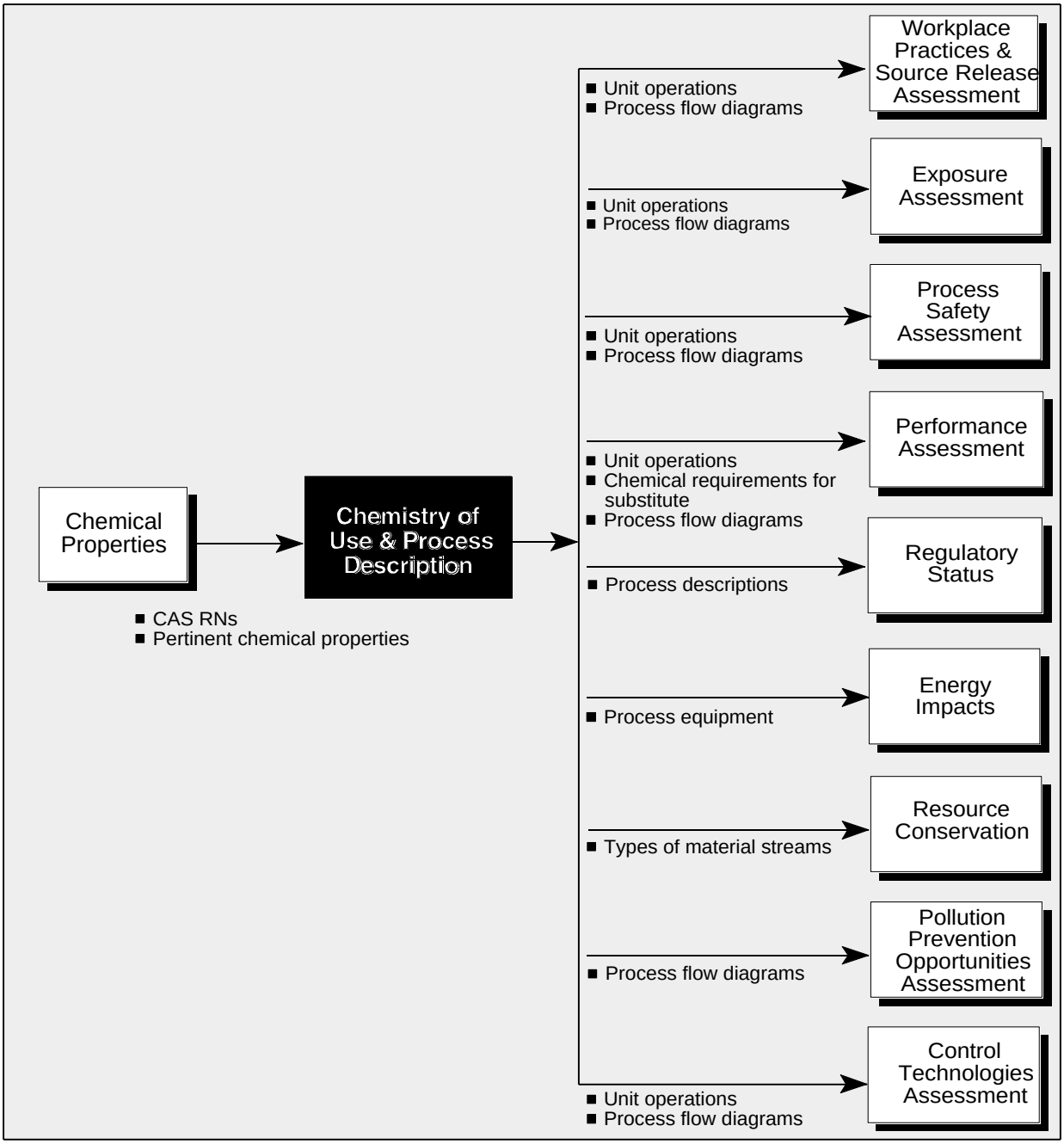
The pattern etching use cluster begins with the chemical etching of the unetched circuit panels and ends with the final drying of the etched panel. The use cluster shown here has the functional subgroups of chemical etching (Subgroup 1) and tin resist stripping (Subgroup 2). Subgroup 1 includes the actual etching step as well as a rinsing step to remove the excess etchant from the panels. Subgroup 2 includes the actual tin-resist stripping process step and a rinsing and drying step performed before the etched circuits can pass to the next step in the printed wiring board manufacturing process.

FIGURE 5-7: EXAMPLE PROCESS FLOW DIAGRAM OF A PATTERN ETCH PROCESS FOR PWB MANUFACTURING



FLOW OF INFORMATION: In a CTSA, this module receives information from the Chemical Properties module and transfers information to the Workplace Practices & Source Release Assessment, Exposure Assessment, Process Safety Assessment, Performance Assessment, Regulatory Status, Energy Impacts, Resource Conservation, Pollution Prevention Opportunities Assessment, and Control Technologies Assessment modules. Example information flows are shown in Figure 5-8.

FIGURE 5-8: CHEMISTRY OF USE & PROCESS DESCRIPTION MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: Although no publications were identified that provide guidance for this module, chemical engineering textbooks explain the basic concepts of process flow diagrams and provide numerous examples. Table 5-17 lists a few examples of chemical engineering textbooks.

TABLE 5-17: PUBLISHED GUIDANCE ON CHEMISTRY OF USE & PROCESS DESCRIPTION

Reference	Type of Guidance
Himmelblau, David M. 1990. *Basic Principles and Calculations in Chemical Engineering*.	Examples of process flow diagrams.
Luyben, William and L. Wenzel. 1988. *Chemical Process Analysis: Mass and Energy Balances*.	Examples of process flow diagrams.

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

DATA SOURCES: None cited.

PROCESS SAFETY ASSESSMENT

OVERVIEW: The Process Safety Assessment module screens potential chemical substitutes to determine if they could potentially pose a safety hazard in the workplace. Process operating characteristics and workplace practices are combined with physical hazard data, precautions for safe handling and use, and other data to determine if implementing a chemical substitute might pose a safety hazard. Safe operating procedures for alternative technologies (equipment) are also considered.

GOALS:

- Obtain information on chemical hazards (reactivity, corrosivity, etc.), proper handling and storage precautions, and proper use guidelines for each chemical formulation or technology being evaluated.
- Compare physical hazard data to process operating conditions and workplace practices to determine if any of the chemical substitutes might pose a safety hazard in the workplace.
- Determine what special actions, if any, need to be taken when using substitute chemicals, formulations, or processes.
- Guide the selection and use of chemicals or processes that are less hazardous in the workplace.

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

- Knowledge of chemicals used and/or produced by the process as well as knowledge and understanding of the technologies and equipment used for the process.
- Knowledge of the workplace practices and operating procedures for the given process.
- Knowledge of process safety analysis, Occupational Safety and Health Administration (OSHA) regulations, and guidelines pertaining to hazardous chemicals and industrial safety.

Within a business or a DFE project team, the people who might supply these skills include a process engineer, safety engineer, safety specialist, or an industrial hygienist.

DEFINITION OF TERMS: The Process Safety Assessment module focuses on physical hazards such as flammability and explosivity rather than health hazards from toxic chemical exposure. Health hazards are characterized in other parts of the CTSA. The definitions of

OSHA established limits for worker exposure to toxic chemicals (e.g., Permissible Exposure Limit and Threshold Limit Value) are listed in this module, however, to assist the individual in interpreting material safety data sheet data.

Combustible Liquid: As defined by OSHA (29 CFR 1910.1200), any liquid having a flash point at or above 140 °F (37.6 °C), but below 200 °F (93.3 °C), except any mixture having components with flashpoints of 200 °F (93.3 °C), or higher, the total volume of which makes up 99 percent or more of the total volume of the mixture.

Compressed Gas: As defined by OSHA (29 CFR 1910.1200):

- A gas or mixture of gases having, in a container, an absolute pressure exceeding 40 psi at 70 °F (21.1 °C).
- A gas or mixture of gases having, in a container, an absolute pressure exceeding 104 psi at 130 °F (54.4 °C) regardless of the pressure at 70 °F (21.1 °C).
- A liquid having a vapor pressure exceeding 40 psi at 100 °F (37.8 °C) as determined by ASTM D-323-72.

Corrosive: As defined by OSHA (29 CFR 1910.1200), a chemical that causes visible destruction of, or irreversible alterations in, living tissue by chemical action at the site of contact. For example, a chemical is considered to be corrosive if, when tested on the intact skin of albino rabbits by the method described by the U.S. Department of Transportation in Appendix A to 49 CFR 173, it destroys or changes irreversibly the structure of the tissue at the site of contact following an exposure period of four hours. According to the OSHA definition, this term shall not refer to action on inanimate surfaces.

Explosive: As defined by OSHA (29 CFR 1910.1200), a chemical that causes a sudden, almost instantaneous release of pressure, gas, and heat when subjected to sudden shock, pressure, or high temperature.

Flammable: As defined by OSHA (29 CFR 1910.1200), a chemical that falls into one of the following categories:

- Flammable aerosol: An aerosol that, when tested by the method described in 16 CFR 1500.45, yields a flame projection exceeding 18 inches at full valve opening, or a flashback (a flame extending back to the valve) at any degree of valve opening.
- Flammable gas:
  - A gas that, at ambient temperature and pressure, forms a flammable mixture with air at a concentration of 13 percent by volume or less; or
  - A gas that, at ambient temperature and pressure, forms a range of flammable mixtures with air wider than 12 percent by volume, regardless of the lower limit.
- Flammable liquid: Any liquid having a flashpoint below 100 °F (37.8 °C), except any mixture having components with flashpoints of 100 °F (37.8 °C) or higher, the total of which make up 99 percent or more of the total volume of the mixture.
- Flammable solid: A solid, other than a blasting agent or explosive as defined in 29 CFR 1910.109(a), that is liable to cause fire through friction, absorption of moisture, spontaneous chemical change, or retained heat from manufacturing or processing, or

which can be ignited readily and when ignited burns so vigorously and persistently as to create a serious hazard. A chemical shall be considered to be a flammable solid if, when tested by the method described in 16 CFR 1500.44, it ignites and burns with a self-sustained flame at a rate greater than one-tenth of an inch per second along its major axis.

Flash Point: As defined by OSHA (29 CFR 1910.1200), the minimum temperature at which a liquid gives off a vapor in sufficient concentration to ignite when tested as follows:

- Tagliabue Closed Tester: (see American National Standard Method of Test for Flash Point by Tag Closed Tester, Z11.24-1979 [ASTM D 56-79]) for liquids with a viscosity of less than 45 Saybolt Universal Seconds (SUS) at 100 ^{o}F (37.8 ^{o}C), that do not contain suspended solids and do not have a tendency to form a surface film under test.
- Pensky-Martens Closed Tester: (see American National Standard Method of Test for Flash Point by Pensky-Martens Closed Tester, Z11.7-1979 [ASTM D 93-79]) for liquids with a viscosity equal to or greater than 45 SUS at 100 ^{o}F (37.8 ^{o}C), or that contain suspended solids, or that have a tendency to form a surface film under test.
- Setaflash Closed Tester: (see American National Standard Method of Test for Flash Point by Setaflash Closed Tester [ASTM D 3278-78].) Typical units are ^{o}C or ^{o}F.

Hazard: A condition or changing set of circumstances that presents a potential for injury, illness, or property damage. The potential or inherent characteristics of an activity, condition, or circumstance which can produce adverse or harmful consequences. Hazards can be categorized into four groups: biological, chemical, mechanical, and physical.

Hazardous Chemical: As defined by OSHA (29 CFR 1910.1200), any chemical which is a physical hazard or a health hazard.

Hazardous Substance: Any substance which has the potential of causing injury by reason of its being explosive, flammable, toxic, corrosive, oxidizing, irritating, or otherwise harmful to personnel.

Immediately Dangerous to Life or Health (IDLH): The maximum inhalation level from which a worker could escape without any escape-impairing symptoms or any irreversible health effects.

Industrial Hygiene: The science and art devoted to the recognition, evaluation, and control of those environmental factors or stresses arising in or from work situations which may cause sickness, impaired health and well-being, or significant discomfort and inefficiency among workers or among the citizens of a community.

Irritant: As defined by OSHA (29 CFR 1910.1200), a chemical which is not corrosive but which causes a reversible, inflammatory effect on living tissue by chemical action at the site of contact. A chemical is a skin irritant if, when tested on the intact skin of albino rabbits by the methods of 16 CFR 1500.41 for four hours exposure or by other appropriate techniques, it results in an empirical score of five or more. A chemical is an eye irritant if so determined under the procedure listed in 16 CFR 1500.42 or other appropriate techniques.

Lower Explosive Limit (LEL): The minimum concentration of combustible gas or vapor in air below which propagation of flame does not occur on contact with a source of ignition. The lower limit of flammability of a gas or vapor at ordinary ambient temperatures expressed in percent of the gas or vapor in air by volume.

Material Safety Data Sheet (MSDS): As defined by OSHA (29 CFR 1910.1200), written or printed material concerning a hazardous material which contains the following:

- The identity of the hazardous material (except as provided for materials that are trade secrets).
- The physical and chemical characteristics of the hazardous chemical (such as vapor pressure, flash point).
- The physical hazards of the hazardous chemical, including the potential for fire, explosion, and reactivity.
- The health hazards of the hazardous chemical, including signs and symptoms of exposure, and any medical conditions which are generally recognized as being aggravated by exposure to the chemical.
- The primary route(s) of entry.
- The OSHA PEL, ACGIH Threshold Limit Value, and any other exposure limit used or recommended by the chemical manufacturer, importer, or employer preparing the MSDS, where available.
- Whether the hazardous chemical is listed in the National Toxicology Program (NTP) Annual Report on Carcinogens (latest edition) or has been identified as a potential carcinogen in the International Agency for Research on Cancer (IARC) Monographs (latest editions) or by OSHA.
- Any generally applicable precautions for safe handling and use which are known to the chemical manufacturer, importer, or employer preparing the MSDS, including appropriate hygienic practices, protective measures during repair and maintenance of contaminated equipment, and procedures for clean-up of spills and leaks.
- Any generally applicable control measures which are known to the chemical manufacturer, importer or employer preparing the MSDS, such as appropriate engineering controls, work practices, or personal protective equipment.
- Emergency and first aid procedures.
- The date of preparation of the MSDS or the last change to it.
- The name, address, and telephone number of the chemical manufacturer, importer, employer or other responsible party preparing or distributing the MSDS, who can provide additional information on the hazardous chemical and appropriate emergency procedures, if necessary.

Mixture: As defined by OSHA (29 CFR 1910.1200), any combination of two or more chemicals if the combination is not, in whole or in part, the result of a chemical reaction.

Occupational Safety and Health Act: Federal statute that governs workplace safety and the exposure of workers to chemicals in the workplace.

Occupational Safety and Health Administration (OSHA): A federal agency under the United States Department of Labor which develops and administers industrial safety and health standards.

Organic Peroxide: As defined by OSHA (29 CFR 1910.1200), an organic compound that contains the bivalent -O-O-structure and which may be considered to be a structural derivative of hydrogen peroxide where one or both of the hydrogen atoms has been replaced by an organic radical.

Oxidizer: As defined by OSHA (29 CFR 1910.1200), a chemical other than a blasting agent or explosive as defined in 1910.109(a), that initiates or promotes combustion in other materials, thereby causing fire either of itself or through the release of oxygen or other gases.

Permissible Exposure Limit (PEL): An enforceable standard promulgated by OSHA. The PEL for a substance is the 8-hour TWA or ceiling concentration above which workers may not be exposed. Although personal protective equipment may not be required for exposures below the PEL, its use may be advisable where there is a potential for overexposure. In many cases, PELs are derived from TLVs published in 1968.

Personal Protective Equipment (PPE): Any material or device worn to protect a worker from exposure to or contact with any harmful substance or force.

Physical Hazard: As defined by OSHA (29 CFR 1910.1200), a chemical for which there is scientifically valid evidence that it is a combustible liquid, a compressed gas, explosive, flammable, an organic peroxide, an oxidizer, pyrophoric, unstable (reactive) or water-reactive.

Pyrophoric: As defined by OSHA (29CFR 1910.1200), a chemical that will ignite spontaneously in air at a temperature of 130 ^{o}F (54.4 ^{o}C) or below.

Reactive: Readily susceptible to chemical change and the possible release of energy; unstable. For example, as defined by OSHA (29 CFR 1910.1200), water-reactive means a chemical will react with water to release a gas that is either flammable or presents a health hazard.

Recommended Exposure Limit (REL): The workplace exposure concentration recommended by the National Institute for Occupational Safety and Health (NIOSH) for promulgation by OSHA as a PEL, but not enforceable as is the OSHA PEL. Typical units are parts per million (ppm).

Sensitizer: As defined by OSHA (29 CFR 1910.1200), a chemical that causes a substantial proportion of exposed people or animals to develop an allergic reaction in normal tissue after repeated exposure to the chemical.

Threshold Limit Value (TLV): The airborne concentration of a substance representing a condition under which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect. Air at such a value may be breathed continually for 8 hours per day and 40 hours per week without harm. Because of wide variation in individual susceptibility,

exposure of an occasional individual at or even below the TLV may not prevent discomfort, aggravation of a preexisting condition, or occupational illness. This is also referred to as the threshold limit value - time-weighted average (TLV-TWA). Typical units are ppm.

Threshold Limit Value - Ceiling (TLV-C): The concentration that should not be exceeded even instantaneously. Typical units are ppm.

Threshold Limit Value - Short-Term Exposure Limit (TLV-STEL): A 15-minute TWA exposure that should not be exceeded at any time during the work day. Typical units are ppm.

Upper Explosive Limit (UEL): The maximum proportion of vapor or gas in air above which propagation of flame does not occur. The upper limit of the flammable or explosive range. See also LEL.

APPROACH/METHODOLOGY: The following presents a summary of the approach or methodology for assessing the process safety of chemical substitutes, processes, and/or technologies. Methodology details for Steps 5, 6, 8, and 9 follow this section.

Step 1: Obtain a MSDS for the chemical products in the use cluster, noting properties of the products, fire and explosion hazard data, reactivity data, precautions for safe handling and use, and control measures. In DfE pilot projects, chemical suppliers have provided MSDSs for the chemical products evaluated in the Performance Assessment. If an MSDS is not available, or a MSDS has not yet been generated for a new substitute chemical product, the information contained within an MSDS should be developed to adequately assess the potential safety hazards of a substitute. (See the resources listed in the Published Guidance on Process Safety, Table 5-19, and Sources of Process Safety Data, Table 5-20.)

Step 2: If a MSDS is not available for a substitute, obtain chemical identities, including CAS RNs and synonyms, and chemical properties for individual chemicals, such as reactivity and flashpoint, from the Chemical Properties module.

Step 3: Obtain the process description and process flow diagram from the Chemistry of Use & Process Description module.

Step 4: Obtain a description of worker activities and workplace practices from the Workplace Practices & Source Release Assessment module.

Step 5: Compare MSDS data against the process description and workplace practices to determine if the substitute chemical might pose a safety hazard.

Step 6: Determine and list special precautions or actions that should be taken if a substitute is used that presents a safety hazard. This information could affect the feasibility or the cost of the process and therefore, whether or not to use that particular substitute.

Step 7: If a substitute is considered a hazardous chemical, refer to OSHA 29 CFR 1910.119 to determine the process safety management of that substitute. This would include using hazard evaluation techniques such as what-if scenarios, checklists, hazard and operability study (HAZOP), failure mode and effects analysis (FMEA), and other analyses. Appendix A to 1910.119 also contains a list of highly hazardous chemicals, toxics, and reactives. (Also refer to Table 5-10 for other sources of published guidance.)

Step 8: Review OSHA regulations to determine and list safe operating procedures, including safe start-up and shut-down procedures, that apply to the baseline or to the substitutes.

Step 9: Provide results of the Process Safety Assessment module to the Cost Analysis and the Risk, Competitiveness, & Conservation Data Summary modules.

METHODOLOGY DETAILS: This section presents the methodology details or examples for completing Steps 5, 6, 8, and 9 above.

Details: Step 5, Comparing MSDS Data with the Process Description and Workplace Practices

The following are examples of chemical properties that may be incompatible with certain operating conditions:

- Flammable chemicals used in an area where welding occurs.
- Flammable chemicals used in a process that operates at elevated temperatures near the chemical flashpoint.
- Water-reactive chemicals used in an area where aqueous spray washing occurs.
- Water-reactive chemicals used in a humid environment where water condenses on chilled equipment.

Details: Step 6, Determining or Listing Special Precautions or Actions to be Taken if Substitute is Used

Examples of special precautions include the following storage conditions:

- Flammable liquids, which should be stored in flammable liquid storage cabinets or refrigerators.
- Caustics, which should not be stored next to acids.

- Oxidizers, which should be stored separately from flammable and combustible materials as well as reducing agents (some oxidizers, such as perchloric acid, must be used only in a water wash-down fume hood made of stainless steel).
- Peroxide-forming compounds, which should be stored in airtight containers in a dark, cool, dry area.
- Compressed gases, which should be stored in a locked, upright position and contained within gas cylinders in a dry, cool location away from fumes, direct and indirect heat or flames.
- Chemicals that are highly flammable or corrosive (hazardous gases must be stored and used in fume hoods or ventilated cabinets and adequate PPE should be used).

Other examples of special precautions to be taken if a substitute presents a safety hazard are the use of chemical protective clothing and respirators. Specific examples warranting the use of chemical protective clothing include:

- Handling liquid chemicals during electronic component manufacture.
- Maintenance and quality assurance activities for chemical production.
- Application of pesticides and other agricultural chemicals.
- Chemical waste handling and emergency chemical spill response.

Specific examples warranting the use of respirators include:

- While engineering controls are being installed or tested.
- While engineering controls are being repaired or maintained; during fire fighting activities.
- During escape from suddenly occurring hazardous atmospheres.
- To eliminate hazardous conditions associated with emergencies.
- For operations where other controls are not feasible.
- For certain short-term operations where installing engineering controls would be economically impractical.

Details: Step 8, Reviewing OSHA Safe Operating Procedures

OSHA has established safe operating procedures that are either industry-specific or apply to the operation of equipment in numerous industry sectors. An example of a widely applicable OSHA standard is 29 CFR 1910.147, the OSHA standard entitled "The Control of Hazardous Energy (Lockout/Tagout)." This standard covers the servicing and maintenance of machines and equipment in which the unexpected energization or start-up of the machines or equipment, or release of stored energy could cause injury to employees. For some types of equipment the standard permits "tagout" or placement of a tagout device on an energy isolating device in accordance with established procedure to warn that equipment may not be operated if the employer can demonstrate that using the tagout will provide full employee protection.

Details: Step 9, Providing Results of the Process Safety Assessment to the Cost Analysis and the Risk, Competitiveness & Conservation Data Summary Modules

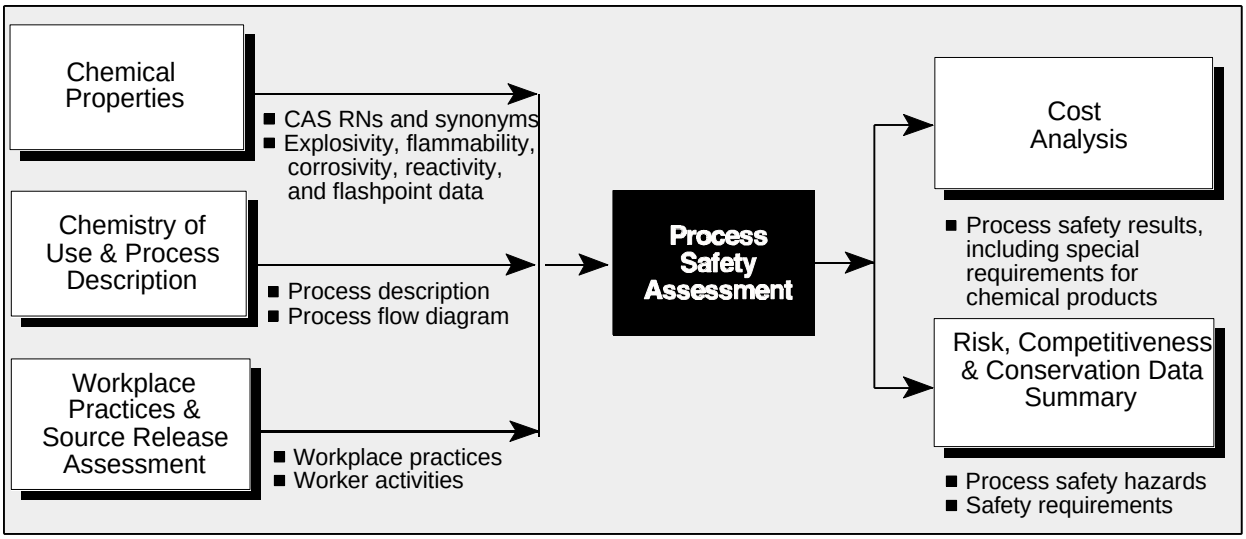
Table 5-18 indicates the type of information transferred from the Process Safety Assessment module.

TABLE 5-18: DATA TRANSFERRED FROM THE PROCESS SAFETY ASSESSMENT MODULE

Module	Data Transferred
Cost Analysis	Whether or not substitute requires special equipment which must be purchased. (Examples would include flammable liquid storage cabinets, fume hoods, ventilated cabinets, and PPE.)
Risk, Competitiveness & Conservation Data Summary	Corrosivity, explosivity, flammability possibilities and whether or not substitute is a hazardous chemical or substance, and a comparison of all substitutes to assess differences in physical or mechanical hazards.

FLOW OF INFORMATION: In a CTSA, this module receives data from the Chemical Properties, Chemistry of Use & Process Description, and Workplace Practices & Source Release Assessment modules. The Process Safety Assessment module transfers data to the Cost Analysis and the Risk, Competitiveness & Conservation Data Summary modules. Example information flows are shown in Figure 5-9.

FIGURE 5-9: PROCESS SAFETY ASSESSMENT MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: Table 5-19 presents references for published guidance on process safety.

TABLE 5-19: PUBLISHED GUIDANCE ON PROCESS SAFETY

Reference	Type of Guidance
American Petroleum Institute. UNDATED. *Management of Process Hazards.*	Describes recommended practices to prevent or minimize process hazards.
Dow Chemical Company. 1987. *Dow's Fire and Explosion Index Hazard Classification Guide.*	Helps the user quantify the expected damage of potential fire and explosion incidents; identifies equipment likely to contribute to the creation or escalation of an incident; and communicates fire and explosion risk potential to management.
National Safety Council. UNDATEDa. *Accident Prevention Manual for Industrial Operations.*	Three volumes containing accident prevention information concerning administration, engineering and technology, and environmental issues.
National Safety Council. UNDATEDb. *Fundamentals of Industrial Hygiene.*	Illustrated reference covers monitoring, evaluation, and control of workplace health hazards. It deals with OSHA regulations, professional standards, exposures, and worker's right to know laws.
National Safety Council. 1983. *Accident Investigation. . . A New Approach.*	Includes a seven-point program to cover environmental issues. Defines the components of a comprehensive program and of regulatory compliance.
Stull, D.R., Ed. UNDATED. *Fundamentals of Fire and Explosion.*	Reviews the fundamentals of fire and explosion. Topics include thermochemistry; kinetochemistry; ignition (gases, liquids, and solids); flames and dust explosions; thermal explosions; gas phase detonations; condensed phase detonations; evaluating reactivity hazard potential; blast effects, fragments and craters; and protection against explosions.
Texas Chemical Council. UNDATED. *Recommended Guidelines for Contractor Safety and Health.*	Includes a comprehensive model for a contractor safety and health program in the chemical industry. Describes responsibilities, safety requirements, safety and health training, safety program, substance abuse, safety audit, and accident reporting.

TABLE 5-19: PUBLISHED GUIDANCE ON PROCESS SAFETY	
Reference	**Type of Guidance**
U.S. Department of Labor, Occupational Safety and Health Administration. UNDATEDa. *The Control of Hazardous Energy (Lockout/Tagout), 29 CFR 1910.147.*	Describes the OHSA regulations for the servicing and maintenance of machines and equipment in which the unexpected energization or start-up of the machines or equipment, or release of stored energy could cause injury to employees.
U.S. Department of Labor, Occupational Safety and Health Administration. UNDATEDb. *Process Safety Management of Highly Hazardous Chemicals, 29 CFR 1910.119.*	Describes the OSHA regulations for process safety management of highly hazardous chemicals.
U.S. Department of Labor, Occupational Safety and Health Administration. UNDATEDc. *Regulations Relating to Labor, 29 CFR 1926.64, Subpart D -- Occupational Health and Environmental Controls*.	Describes the OSHA regulations for preventing or minimizing the consequences of catastrophic releases of toxic, reactive, flammable, or explosive chemicals.
U.S. Department of Labor, Occupational Safety and Health Administration. UNDATEDd. *Regulations Relating to Labor, 29 CFR 1910, Subpart Z -- Toxic and Hazardous Substances*.	Describes the OSHA regulations for hazard communication.
U.S. Department of Labor, Occupational Safety and Health Administration. UNDATEDe. *Training Requirements in OSHA Standards and Training Guidelines*.	Describes OSHA training guidelines and requirements for general industry, maritime, construction, agricultural, and federal employees.
U.S. Department of Labor, Occupational Safety and Health Administration. 1970. *Occupational Safety and Health Act of 1970, Public Law No. 91-596.*	Describes original OSHA statute.
U.S. Department of Labor, Occupational Safety and Health Administration. 1986. *Safety & Health Guide for the Chemical Industry*.	Contains guidelines used by OSHA compliance officers to evaluate employer safety programs, particularly in the areas of disaster prevention and emergency response.
U.S. Department of Labor, Occupational Safety and Health Administration. 1989b. *Chemical Hazard Communication*.	Contains a summary of the OSHA Hazard Communication Standard.
U.S. Department of Labor, Occupational Safety and Health Administration. 1993. *Process Safety Management Guidelines for Compliance*.	Describes a systematic approach to designing a process safety management program.
U.S. Department of Transportation. UNDATED. *Hazardous Materials Transportation Regulations, 49 CFR 100 to 177*.	Lists and describes hazardous materials as well as requirements for shipping, labeling, and transporting hazardous materials.

TABLE 5-19: PUBLISHED GUIDANCE ON PROCESS SAFETY	
Reference	**Type of Guidance**
U.S. Department of Transportation. 1994. *Emergency Response Guide.*	Lists chemicals which are health hazards and the emergency measures needed in the events of fire, explosion, injury, spills, and accidental releases.

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

DATA SOURCES: Table 5-20 lists sources of process safety data.

TABLE 5-20: SOURCES OF PROCESS SAFETY DATA	
Reference	**Type of Data**
Hazardous Chemicals Data Book. 1986.	Includes the following data on certain hazardous chemicals: chemical description, fire and explosion hazards, life hazards, personal protection needed, fire fighting measures, usual shipping containers, storage information, and special remarks regarding electrical installations and NFPA code numbers pertaining to the specified chemical.
Merck Index. 1989.	Handbook containing some caution and/or human toxicity statements for some substances.
National Fire Protection Association. 1995. *Fire Protection Guide on Hazardous Materials.*	Includes complete text of four different fire codes. Also includes chemical hazard data, quantitative health hazard rating based on recent research, and information needed on handling and storage of hazardous chemicals.
NIOSH/OSHA Pocket Guide to Chemical Hazards. 1995.	Lists known hazardous chemicals along with their health hazards, exposure limits, chemical and physical properties, incompatibilities, and suggested PPE, including recommended respirators.

TABLE 5-20: SOURCES OF PROCESS SAFETY DATA	
Reference	**Type of Data**
Sax, N. Irving and Richard J. Lewis, Sr. 1989. *Dangerous Properties of Industrial Materials*.	A three-volume set containing hazard information. Volume I contains essays on selected topics relating to hazardous materials, a CAS RN cross-index, a synonym cross-index, and the list of CODEN bibliographic references given in the data section. Volumes II and III list and describe more than 20,000 materials in alphabetical order by entry name. Descriptions include physical and chemical properties, clinical data on experimental animals and humans, a material's hazard potential, IARC Cancer Review and the U.S. National Toxicology Program cancer testing program conclusions, OSHA PELs, ACGIH TLVs, and NIOSH RELs, DOT classifications, and Toxic and Hazardous Reviews (THRs). Fire and explosion hazards are briefly summarized.
Threshold Limit Values for Chemical Substances and Physical Agents in the Work Environment. UNDATED.	Lists TLVs for many chemicals found in the workplace.

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

MARKET INFORMATION

OVERVIEW: The market information module contains economic data used to evaluate the importance of the target industry sector to the overall market for the alternatives under review, and conversely, the economic importance of the alternatives to the industry sector. Market information includes chemical/technology cost information, production and manufacturing volumes, chemical/technological use breakdowns, and an analysis of market trends that could affect future supply and demand.

GOALS:

- Evaluate the importance of the target industry sector to the overall market for the baseline and alternative chemicals and technologies.
- Compile price information for the baseline and alternatives to be used in the Cost Analysis module.
- Identify trends in the manufacturing and use of the baseline and alternatives that may influence future supply and demand.
- Compile information for the International Information module.

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

- Knowledge of market information data sources and the capability to evaluate market trends.

Within a business or a DfE project team, the people who might supply these skills include a purchasing agent or an economist. Vendors of the chemicals or technologies may also be a good resource.

DEFINITION OF TERMS: Not applicable.

APPROACH/METHODOLOGY: The following presents a summary of the technical approach or methodology for the Market Information module.

Step 1: Obtain chemical CAS RNs and synonyms from the Chemical Properties module.

Step 2: Using the most current data available, determine the total volumes of the chemicals and chemical products produced both in the U.S. and internationally, volumes imported and exported, volumes used by the target industry, and the names and

locations of current producers (see Table 5-21: Sources of Market Information). Some of this information will have been collected in the Industry and Use Cluster Profile, but chemical use volumes may be unavailable or considered proprietary.

When data are unavailable, a project team may estimate information so that the transfer of information to other modules will occur. Appendix F gives a detailed example of how chemical volumes were estimated in the screen reclamation use cluster.

Step 3: For the baseline and/or alternative technologies and processes, identify the size of the market for the technology both in the U.S. and internationally, quantities exported and imported, quantities used by the target industry, and the names and locations of manufacturers within the U.S. and internationally.

Step 4: Transfer information on chemicals or technologies primarily supplied by manufacturers outside of the U.S. to the International Information module. Information on international trade issues, as well as source, availability, and cost data for these alternatives are compiled in the International Information module.

Step 5: Collect market price information for the baseline and alternative chemicals and technologies produced in the U.S. from the appropriate chemical or equipment vendors. Transfer market price information to the Cost Analysis module.

Step 6: Evaluate the importance of the target industry to the overall market for the baseline and alternatives in the use cluster. If the industry is a major market for an alternative (i.e., the amount of chemical produced fluctuates in response to the demand for the chemical in this industry; a technology was specifically developed and marketed for the target industry, etc.), consider evaluating the environmental impacts of upstream processes, such as the chemical manufacturing process, in the CTSA.

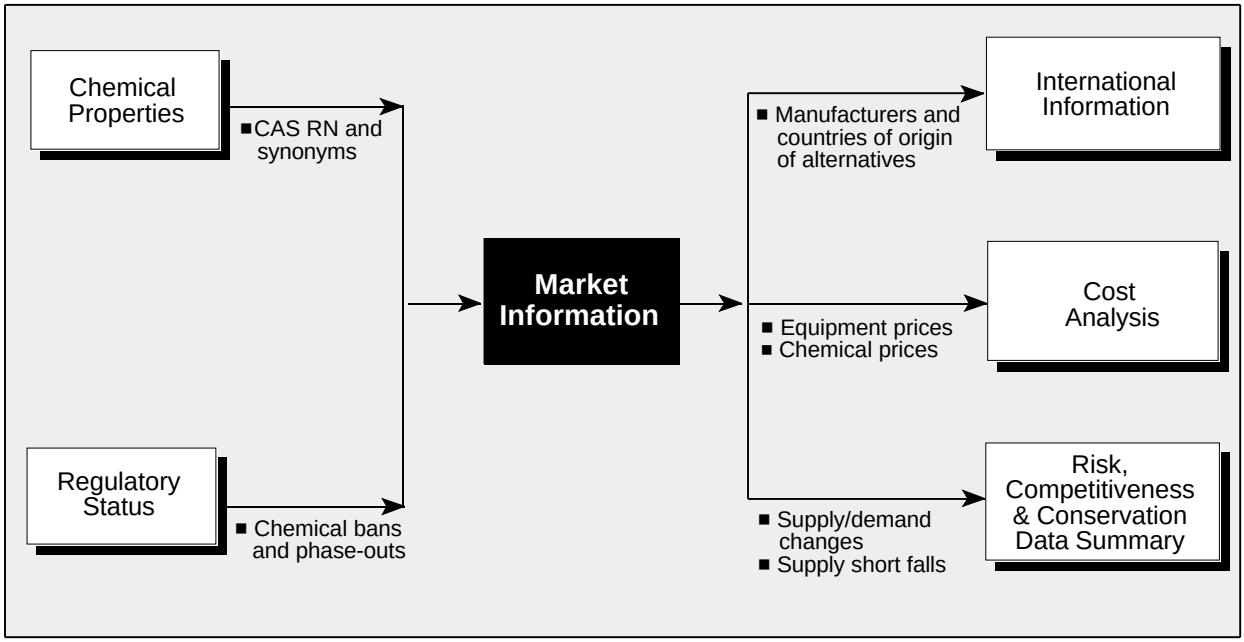
Step 7: Identify factors that could potentially affect the future supply or demand of the baseline or substitutes produced in the U.S. Possible factors include, but are not limited to:

- Proposed legislation on the manufacturing or use of a use cluster chemical, such as bans or phase-outs (see the Regulatory Status module).
- Any recent or expected improvements in technologies that could affect the future demand for a substitute in the target industry or in other industries.
- Resource or production limitations.

Step 8: Transfer any information about expected changes or shortfalls in the supply or demand for the baseline and alternative chemicals and technologies to the Risk, Competitiveness & Conservation Data Summary module.

FLOW OF INFORMATION: The Market Information module receives data from the Chemical Properties and Regulatory Status modules and transfers information to the International Information, Cost Analysis, and Risk, Competitiveness & Conservation Data Summary modules. Example information flows are shown in Figure 5-10.

FIGURE 5-10: MARKET INFORMATION MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: None cited. EPA risk management documents (Preliminary Life-Cycle Analysis and Pollution Prevention Assessment reports) provide examples of the types of market information collected during the second phase of EPA risk management assessments.

DATA SOURCES: Table 5-21 lists sources of market information.

TABLE 5-21: SOURCES OF MARKET INFORMATION

Reference	Type of Data
Chemical Business News Data Base. Updated Periodically.	Data base containing chemical market trends.
Chemical Economics Handbook. Updated Periodically.	Chemical volume and consumption data.

TABLE 5-21: SOURCES OF MARKET INFORMATION	
Reference	**Type of Data**
Chemical Industry Notes Data Base. Updated Periodically.	Data source for chemical industry production and trends.
Chemical Marketing Reporter. Updated Periodically.	Profiles of chemicals containing production data and market trend information.
Directory of Chemical Producers: United States Producers. Updated Periodically.	Chemical production information including manufacturers and production data.
Kirk-Othmer Encyclopedia of Chemical Technology. Updated Periodically.	Chemical production information including manufacturers and production data.
Mannsville Chemical Products Synopsis. Updated Periodically.	Chemical volume and consumption data.
Mines Data Base. Updated Periodically.	Data source for raw mineral and metal production.

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

INTERNATIONAL INFORMATION

OVERVIEW: The International Information module collects data pertaining to the use or production of alternatives in other parts of the world, the impact of international trade on the selection of alternatives, and the impacts of switching to an alternative on international trade. Primarily, the international trade issues are driven by the source and availability of alternatives, and possible indirect costs (e.g., taxes, tariffs, or prohibitions) imposed on alternatives.

GOALS:

- Identify alternatives in use or attempted in other countries and the reasons for using or not using the alternatives.
- Identify the alternative chemicals and technologies in use in the U.S. that are primarily supplied by international sources.
- Identify possible trade implications concerning use of alternatives.
- Understand how trade implications impact availability and the relative social benefits/costs of alternatives.

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

- Ability to search data bases, government agencies, trade association literature, government documents, international organizations, and trade agreements to identify alternative chemicals and technologies used in other countries and to determine the source of the alternatives.
- Knowledge of international trade regulations, agreements and treaties, and ability to determine the international trade implications of selections of particular alternatives.

Within a business or a DfE project team, the people who might supply these skills include a purchasing agent, an economist, or an attorney.

DEFINITION OF TERMS: Not applicable.

APPROACH/METHODOLOGY: The following presents a summary of the approach for collecting international data and identifying international issues that could influence the selection of a substitute. Methodology details for Steps 1, 2, and 5 follow this section.

Step 1: Identify the countries of interest that contain a large target industry sector. Service-oriented businesses such as the dry cleaning industry will most likely be present in almost all industrialized countries. Other industries, such as the printed wiring board industry, may be concentrated in certain regions of the world (i.e., in Asia, North America, etc.).

Step 2: Identify the alternatives that are being used or have been tried in the countries identified in Step 1. If these alternatives differ from those of the U.S., identify the conditions driving the choice of alternatives, such as the presence or absence of regulations. This information may be useful for planning for the future and for spotting trends, including treatment by a national government of chemicals of concern. If new alternatives are identified in this step, the project team will need to decide whether they should be quantitatively evaluated in the CTSA.

Step 3: Review the Market Information module to obtain data on the manufacturers/countries of origin of alternative chemicals, products, or technologies being evaluated in the CTSA.

Step 4: Investigate potential international sources of alternatives with particular attention to the following:

- Production capacity, the capability of producers of meeting market demand, and the stability of pricing structures.
- The price of chemicals and/or technologies supplied by foreign sources.
- Potential problems arising from reliance on foreign suppliers, including additional costs, such as taxes or tariffs, which may make imported alternatives more expensive than domestic.

Step 5: Investigate international trade regulations, agreements, and treaties for their impact on the chemicals or technologies. Examples of international trade agreements include the General Agreement on Tariffs and Trade (GATT) and the North American Free Trade Agreement (NAFTA).

Step 6: Provide the price of chemicals and/or technologies primarily supplied by foreign sources to the Cost Analysis module. Market price information should reflect the suppliers price plus any additional costs, such as international taxes or tariffs or shipping costs.

Step 7: Based on the information collected in Steps 1 through 5, assess the relative social benefits and costs, including the potential indirect costs of selecting an alternative. Indirect costs of alternatives only supplied by international sources might include taxes, tariffs, or prohibitions in addition to foreign relations conflicts or loss of U.S. jobs. International bans or prohibitions on chemicals or technologies could affect a company's ability to market products made with that technology.

Alternatives that have been discontinued in some countries may have less stable pricing structures.

Step 8: Provide information on source, availability, and possible indirect costs of the alternatives to the Risk, Competitiveness & Conservation Data Summary module.

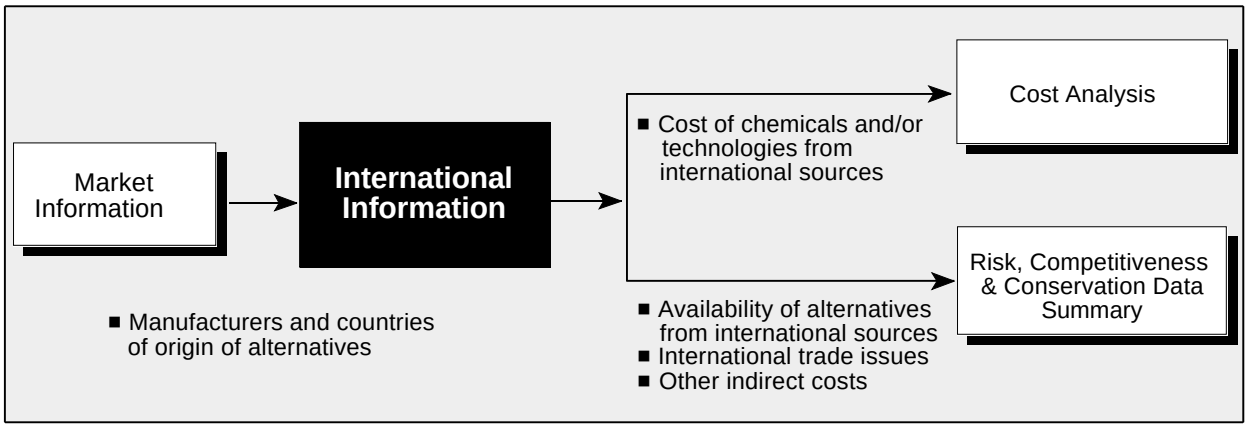
METHODOLOGY DETAILS: This section presents methodology details for completing Steps 1, 2, and 5.

Details: Steps 1, 2, and 5, Identifying Countries of Interest, Alternatives in Use, and International Trade Regulations, Treaties, or Agreements

Trade associations and chemical and equipment suppliers may be good resources for international manufacturing or market share data. Federal agencies and programs that may be able to provide information include the U.S. Department of Commerce, the U.S. Agency for International Development, the U.S. Trade and Development Program, and the U.S. Trade Representative. International organizations include the Organization of Economic Co-operation and Development, the United Nations Conference on Trade and Development, the United Nations Development Program, the United Nations Environment Program, the World Trade Organization, and the World Bank.

FLOW OF INFORMATION: The International Information module receives data from the Market Information module and transfers data to the Cost Analysis and Risk, Competitiveness & Conservation Data Summary modules. Example information flows are shown in Figure 5-11. If new alternatives are identified, the project team must decide whether to include them in the detailed analyses of the CTSA. If so, these alternatives must be returned to the beginning of the CTSA process.

FIGURE 5-11: INTERNATIONAL INFORMATION MODULE: EXAMPLE INFORMATION FLOWS



ANALYTICAL MODELS: None cited.

PUBLISHED GUIDANCE: None cited.

DATA SOURCES: Table 5-22 presents references for data bases, published literature, and government contacts.

TABLE 5-22: SOURCES OF INTERNATIONAL INFORMATION

Reference	Type of Data
Brownson, Ann L., Ed. 1994. *Federal Staff Directory/1*.	Directory of federal programs, services and data bases such as the U.S. Department of Commerce Trade Data Services; U.S. Department of Commerce International Data Base, Census Information; and contacts within the U.S. International Trade Commission. Federal trade services and databases are useful for collecting international information, and for identifying addresses and telephone numbers of international organizations.
Russell, John J., Ed. 1994. *National Trade and Professional Associations of the United States*.	Directory of U.S. Trade Associations representing various industry sectors, including associations aimed at expanding international trade. (For example, the U.S. - ASEAN Council for Business and Technology strives to expand trade between the U.S. and Southeast Asia.)
U.S. Congress. 1992. *Trade and Environment: Conflict and Opportunities*.	Background paper describing the potential for conflict between trade and the environment, as reflected in disputes about the trade impacts of environmental laws and about the environmental impacts arising from efforts to liberalize trade and investment.

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