# Chapter 5 Analysis for a Multisource Assessment

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## 5.0 Introduction

At the end of the planning and scoping process described in Chapter 4, the key stakeholders will have: (1) agreed to the scope of the assessment, (2) signed off on both the conceptual model for the study area and the analytical plan, and (3) created a problem statement that clearly articulates the perceived problem, how it will be studied, and what will not be studied. This chapter discusses the details of the next step in the overall process – the analysis phase (see Exhibit 5-1). Chapter 6 describes how to use the information developed during the analysis phase to create quantitative and qualitative expressions of risk.

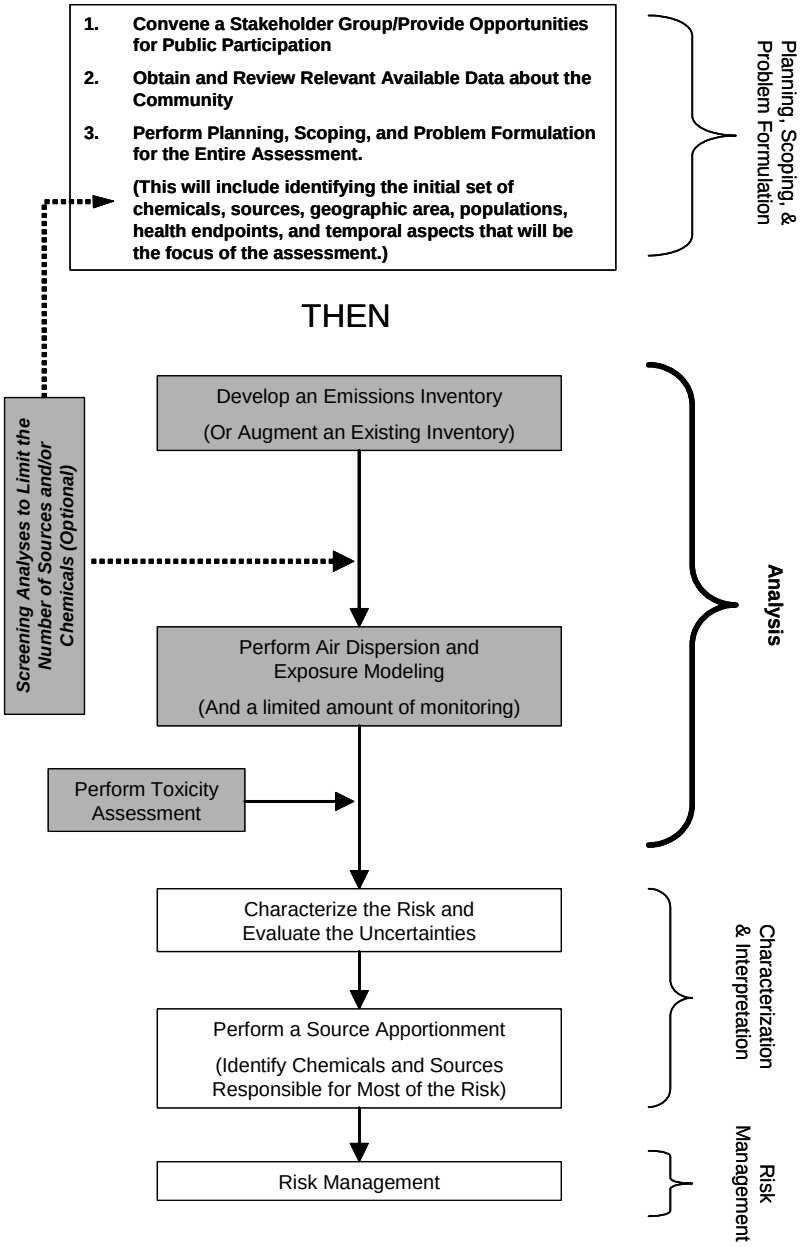
As mentioned in Chapter 4, the methodology described in this resource document focuses on use of air dispersion modeling to estimate ambient concentrations, with monitoring data used primarily for secondary purposes such as evaluation of the modeling results (e.g., comparing to local NATTS or other special study monitors). The dispersion modeling results may be used as a generally conservative surrogate for exposure (a screening level approach, although in some cases ambient concentrations may underestimate actual exposures). In contrast, the risk analysts may decide to take the air dispersion modeling results and use them to develop refined estimates of exposure by the application of an exposure model such as HAPEM (see Exhibit 5-2). ATRA Volume 1, Chapter 11 discusses use of exposure modeling for refined air toxics risk assessments.

There are any number of paths that a given assessment may take to assessing multisource impacts in a given place; there is no "one size fits all" cookbook approach that will work in all cases. The approach ultimately taken depends on the needs of the risk managers (e.g., how thorough an understanding of the problem they need) and the resources available to the analysts. Some assessments, for example, will use a number of simplifying, yet conservative, assumptions to derive risk estimates (e.g., the exposure concentration for the entire study area population is represented by the concentration at the maximum impact location), while other assessments may rely on higher levels of analysis (e.g., probabilistic approaches) to derive a more thorough understanding of the problem. Nevertheless, there are certain elements of the multisource analysis process that will generally be common to most multisource assessments, and this chapter provides an overview of both these common elements and the general process flow that most assessments follow (see an example process flow in Exhibit 5-3).

It should also be noted that there are a variety of tools and models that can be used to accomplish the Exhibit 5-1 analysis tasks. These tools can range in complexity, refinement, and data requirements, and the planning process will have to identify the right tools for the job. In this chapter, the RAIMI methodology and certain other frequently used tools are presented as examples. For some assessments and situations, other less or more refined tools may be appropriate.

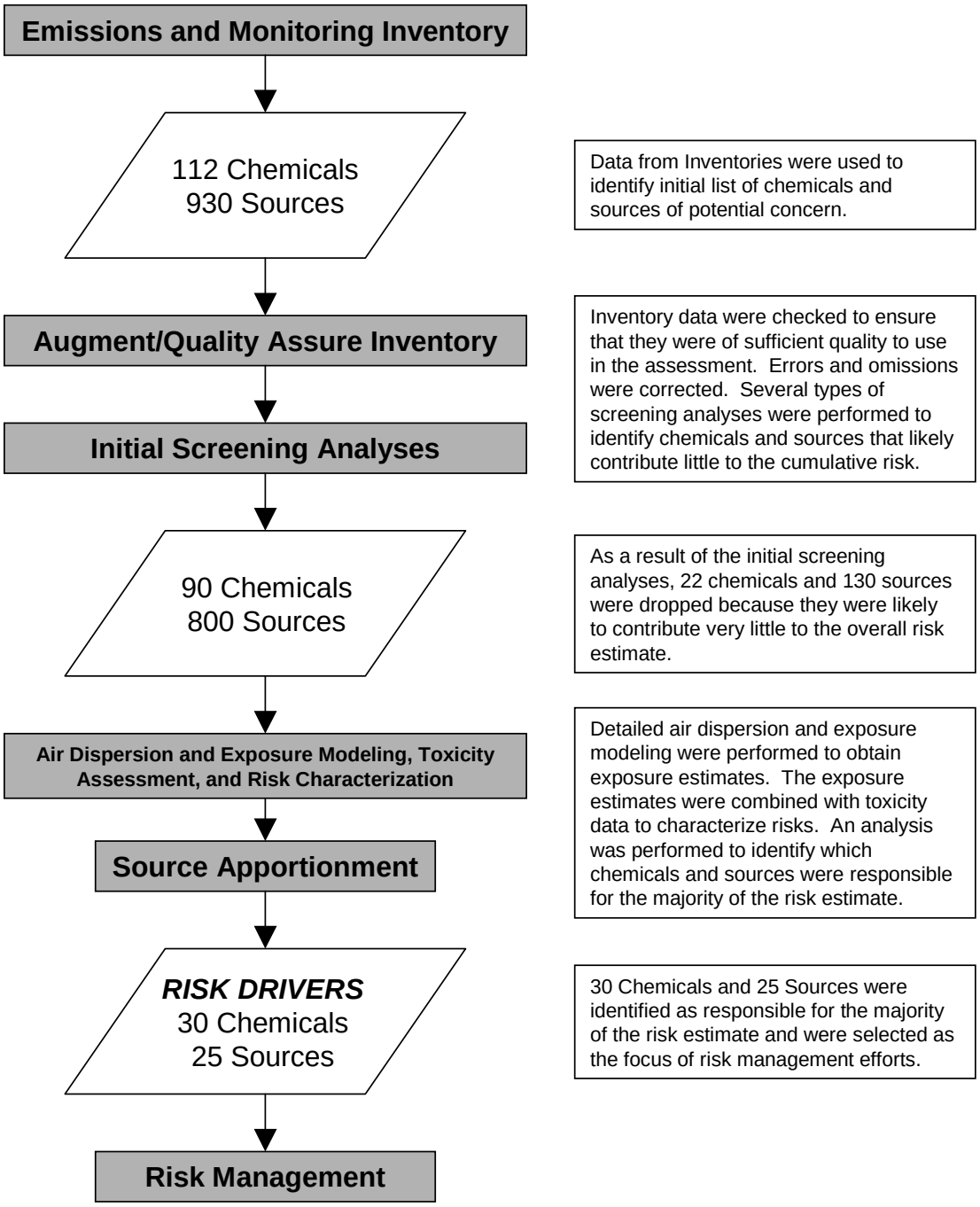
In addition to an overview of the general analytical framework described in this chapter, Appendix B provides the details of some of the common screening techniques that assessors may select to help narrow the focus of the assessment to the most important sources and chemicals.

**Exhibit 5-1. The General Multisource Air Toxics Risk Assessment Process For a Community Assessment – Focus on Analysis**



| Exhibit 5-2. Approaches to Evaluating Exposure | |
|---|---|
| For air toxics impact analysis, a variety of measures may be used to evaluate the potential exposures of a person to a chemical in the air. Some measures are fairly crude and some are more refined. The most common measures used to estimate exposure are listed below (generally, from most crude to most refined): | |
| **Pounds Released** | A very crude indicator of potential exposure because there is no information on toxicity or fate and transport in the environment or on how people interact with the contaminated air. |
| **Toxicity-weighted** | Pounds released of each pollutant, adjusted for its relative carcinogenic potency or reference level for noncancer effects. This measure accounts for toxicity, but not fate and transport or exposure. |
| **Ambient Concentration** | A better indicator of potential exposure (fate and transport are included) but still lacks information on how people interact with the contaminated air. The quality of the concentration estimate depends on the method used to develop it (e.g., the various types of monitoring or modeling used, the quality of the emissions inventory, etc.). |
| **Exposure Model Refined Ambient Concentration** | An even better indicator of potential exposure because it does include information on how people interact with the contaminated air (e.g., do they remain in the immediate area constantly or do they move to areas with differing concentrations). The quality of the information depends on both the methods used to estimate ambient concentration and those used to evaluate demographics and behavior. |
| **Personal Exposure** | An even higher level of understanding of exposure, usually developed by personal exposure monitoring. |
| The term *exposure concentration* is used to describe the concentration of a chemical in its transport or carrier medium (i.e., an environmental medium or contaminated food) at the point of contact. This concentration can be either a monitored or modeled value and may or may not have been refined by the application of an exposure model. | |

**Exhibit 5-3. Example Flow Diagram for a Cumulative Multisource Assessment**



The overall framework for the multisource analysis phase has four key components:

- Emissions characterization (Section 5.1);
- Air dispersion modeling (Section 5.2);
- Estimating inhalation exposure (Section 5.3); and
- Toxicity assessment (Section 5.4).

The remainder of this chapter discusses each of these elements in detail. It should be noted that the information provided here augments the general information on these topics already provided in ATRA Volume 1 by emphasizing some of the key objectives and procedures that are used to perform a community-level multisource assessment.

## 5.1 Emissions Characterization

Emissions characterization (also commonly referred to as source characterization) is simply the development of information about the chemicals that are released to the air in the study area, including chemical identity, location of release, the pattern of release (e.g., continuous, intermittent, burst, etc.) and the physical characteristics of the release. The product of the emissions characterization step is a database of the collected information called the **emissions inventory** (see Section 4.2.1.2). [Since the local mix of sources, chemicals, and other factors (e.g., meteorology) will vary from place to place, the sources and chemicals ultimately found to be responsible for the majority of the risks can also vary from place to place. It is for this reason that the inventory developed for the location-specific multisource assessment initially include information on all important sources of air toxics impacting the study area. At a minimum, this will generally include both mobile sources and stationary sources.]

**Emissions Characterization**
**What Should I Know Before I Proceed?**

To perform the emissions characterization step correctly, analysts should have a strong understanding of several key topics, including:

- The types of chemicals that are considered "air toxics;"
- The types of activities that result in emissions of air toxics, such as industrial and commercial activities, fuel combustion, mobile sources, and use of consumer products;
- The available emission inventories of air toxics, such as the National Emission Inventory (NEI), the Toxic Release Inventory (TRI), and more locally developed inventories; and
- The tools and steps used to develop an emission inventory (or to augment an existing inventory) for use with the selected air dispersion model.

An overview of these subjects is provided in ATRA Volume 1, Chapters 4 and 7. The *How To Manual* (Section 3.5.1) also contains discussions on this topic.

The emissions inventory is one of the key inputs needed by the air dispersion model in order for the model to generate ambient air concentration estimates at the points selected by the analyst. Another key piece of information needed for the modeling effort is meteorological data.

Depending on the air dispersion model employed, different types of emissions inventory data (such as different types of emissions parameters) may be required. The discussion here provides examples of the parameters that are needed for a commonly used Gaussian plume model [the

Industrial Source Complex (ISC) model]. If an alternate dispersion model is used, the requirements of the emissions inventory may be different.

### 5.1.1 Development of Emissions Estimates - The Basics

For a multisource assessment, the analysts will commonly begin the process of (1) developing emissions estimates by obtaining the available emissions inventories for the study area – this will usually be the NEI and the TRI or, in some cases, a more refined state or local emissions inventory; and then (2) refining the inventory, as necessary, according to the data quality objectives (DQOs) that were established in the planning and scoping (planning and scoping) phase (see Chapter 4). In short, the analysts will look at what has already been developed and ask themselves the question, "Is the existing inventory good enough or do we need to refine the inventory to meet the DQOs established during planning and scoping?"

For example, if the planning and scoping process determined that all air toxics emissions reported to the NEI and the TRI would be the focus of the air dispersion modeling analysis, then using the NEI "as is" may not be sufficient. This is because HAP emissions from TRI sources are usually included in the NEI, but non-HAP emissions from TRI sources generally are not. The NEI would needed to be augmented to include the non-HAP air releases reported to the TRI in order to meet the DQOs for emissions estimates established during planning and scoping. More information on common DQOs for the emissions estimate step is provided below.

In some cases, further refinement of the inventory may need to be conducted for high risk pollutants after a screening-level risk assessment has been conducted. This step allows the analyst to focus resources and in-depth analysis efforts on those emission sources likely to have the highest impact on a community.

### 5.1.2 Emissions Characterization DQOs

Exhibit 5-4 presents some of the main emissions data that are needed when using ISC as the air dispersion model for sources in a community-scale multisource assessment. Some examples of the type and nature of DQOs for these data elements might be:

- **Accuracy**: Emission totals are accurate to within some acceptable range (e.g., ±25 percent when compared to sources such as emissions monitoring data, emissions from similar units at different facilities, emissions reported to multiple databases, historically reported emissions at the facility, estimated emissions generated using information in the literature such as industry-specific emissions profiles);

- **Completeness**: All sources emitting at least X tons/year of the compound within some specified distance of the study area boundary (e.g., 1 mile);

- **Completeness**: Emission totals for each source during an annual period;

- **Level of detail**: Emission sources stratified by Standard Classification Code (SCC) and AIRS area and mobile system (AMS) codes;

**Exhibit 5-4. Example Input Data for Characterizing Emissions Sources for Use with the ISC Dispersion Model**

| | Stack Sources | Fugitive Sources | Flare Sources[a] | Mobile Sources[b] |
|---|---|---|---|---|
| Emission Source Parameters | - Stack height [m]<br>- Base elevation [m]<br>- Stack diameter [m]<br>- Stack gas exit velocity [m/s]<br>- Stack gas exit temp. [K]<br>- Horizontal discharge<br>- Location [NAD-83] | - Source area [$m^2$]<br>- Source volume [$m^3$]<br>- Release height [m]<br>- Base elevation [m]<br>- Location [NAD-83] | - Gas flow rate [SCFM]<br>- Average of lowest heats of combustion for flare feed stream constituents (BTU/SCF)<br>- Molecular weight, average for flare constituents<br>- Release height [m]<br>- Base elevation [m]<br>- Location [NAD-83] | - Source area [$m^2$]<br>- Release height [m]<br>- Base elevation [m]<br>- Location [NAD-83] |
| Emissions Data | - Contaminant CAS number and name<br>- Actual annual speciated emission rate [g/s]<br>- Allowable (permitted) emission rate [g/s]<br>- Historical speciated emission rates [g/s] and corresponding reporting year | | | |
| Emission Source Attributes | - State registration or account number for the facility<br>- Company name, and name of the industrial facility<br>- Nearest city and county<br>- Date of most recent emissions data<br>- Emissions point name and ID number<br>- Name and ID of the process facility generating the emissions<br>- Emissions permit number<br>- Source classification code (SCC) | | | |

**Table notes:**

[a] Flare sources, which are modeled as stacks in this example, can be reported as stacks or with other parameters which enable them to be modeled as stacks following conversion calculations.

[b] Mobile sources in this example have been modeled as an area source (e.g., to cover a segment of a major highway). Some of the emissions data and attributes listed here would not apply to mobile sources (e.g., facility name, permit number). Modeling of mobile sources, including a discussion of spatial allocation of such sources, are discussed in more detail in Section 5.1.3.5.

| | | | |
|---|---|---|---|
| m: | meters | NAD-83: | North American Datum 1983 |
| $m^2$: | square meters | BTU/SCF: | British thermal units per standard cubic foot |
| m/s: | meters/second | SCFM: | Standard cubic feet per minute at 68° F |
| g/s: | grams/second | CAS: | Chemical Abstract Service |
| K: | Kelvin | | |

*Source*: http://www.epa.gov/earth1r6/6pd/rcra_c/raimi/raimi.htm

***Note:*** *This exhibit is not meant to be a comprehensive summary of all inputs required by ISC to complete a model run, and some data types listed here are not directly required by ISC (e.g., nearest city and county).*

- **Level of detail**: Spatial resolution of non-point source emissions to some acceptable geographic subdivisions (e.g., US Census tracts, 2-km grid squares); and

- **Level of detail:** Understanding of the temporal nature of emissions data (are they provided as an annual aggregate, as continuous emissions estimates, as intermittent emissions estimates, etc.). Will the emissions data allow an assessment of the exposure duration of interest? For example, data provided as an annual aggregate will provide limited information for acute exposure assessment, but are usually adequate for evaluating chronic exposures.

Other elements that might be considered in establishing an acceptable level of data quality might include:

- Verification and correction of source locations;
- Verification that all chemicals of interest (both HAP and non-HAP) have been included;
- Acceptable level of chemical speciation of the emissions being released; and
- Spatial allocation of non-point emissions to specific locations for dispersion modeling, if needed.

Approaches that can help meet these emissions characterization DQOs are discussed in the following sections.

### 5.1.3 Inventory Review and Augmentation

As mentioned above, there will usually be some emission information available for the study area from an existing inventory (e.g., the NEI or state/tribal/local inventory); however, review and refinement of the information will usually be required to create a study area-specific inventory that meets the study-specific DQOs. This section discusses some of the areas of refinement that are commonly needed in the development of the emissions inventory for the community-scale assessment.

#### 5.1.3.1 Preparing Emissions Data for Assessment Purposes

Depending on what use the emissions data will be put to (e.g., as an input to a dispersion model), there may be different requirements for both the content of the emissions inventory as well as the format of the inventory (e.g., a particular database or file structure). The user's guides for the various air dispersion models should be consulted to insure that the emissions inventory development process will meet both the content and the file structure requirements for the selected model. For example, the emissions inventory database structure used in the RAIMI process (which can be developed with the assistance of the RAIMI "Data Miner Tool;" see text box below) is shown in Appendix C. Other models (e.g., HEM-Screen, CalPUFF, etc.) will have other emissions parameter and file formatting requirements.

In addition to creating the emissions file or database in the required format, some additional processing and management of calculated or revised source characterization data are often required to support the modeling analysis. Typical examples of further processing of source characterization data include the following:

- **Conversion of Reported Units**: Certain source characterization data may require conversion of reported units into alternate units to ensure accurate use in algorithms applied in source and risk characterization. Parameters for which conversions are typically required include release heights, source dimensions, stack gas exit parameters, etc. For example, the ISCST3 model requires that stack height be input in meters; therefore, heights reported as feet in an emission inventory would need to be converted (i.e., 1 foot = 0.3048 meters). Another parameter for which conversions are typically required include emission rates (such as actual and allowable emission rates being changed from tons per year to grams per second).

- **Calculation of Source Terms for Source Modeling of Emission Sources**: Certain source characterization data may be utilized in the calculation of additional emission source parameters for modeling fugitive and flare sources. For example, fugitive emissions from equipment leaks may be modeled as a representative volume source with the approximate dimensions of the entire area in which the pipes, flanges, valves, and other sources of equipment leaks are located, and operating conditions (hours of operation, flow rates, etc.) could be used to refine the emission rate and other required parameters. Calculated source

**Automating the Process – Emissions Inventories**

Modeling and cumulative-type risk assessment projects require inspection and analysis of large emissions inventory databases. Because there are numerous relational database possibilities, each having many fields, it can take significant time to track down particular details embedded in this mass of information. In addition to the complexity of the information, many applications are unable to handle the massive volumes of data. For example, common desktop software such as Microsoft Excel® cannot handle more than 65,600 rows of data.

The **RAIMI Data Miner** is one tool that helps the analyst overcome these limitations. This is a large database client-server processing system that facilitates the assembly of multi-source emissions inventories for air and risk characterization. With Data Miner, you can:

- Create and edit database table relationships and views for complete access to all emissions attributes maintained in the database;
- Link source-specific parameters necessary for air and risk characterization from multiple database tables through the Data Organizer component; and
- Extract the source-specific data sets by constructing and executing simple or complex data queries in the Query Builder component.

For more information on the RAIMI Data Miner, see:
http://www.epa.gov/Arkansas/6pd/rcra_c/raimi/raimi.

Other tools are also available that may be more appropriate depending on the needs of the assessment. For example, EPA's Emissions Modeling System for Hazardous Air Pollutants (EMS-HAP) (http://www.epa.gov/scram001/dispersion_related.htm#ems-hap), which has been used to process emissions data and source parameters used in EPA national-scale assessments, is useful for particularly large applications. For smaller-scale assessments, desktop spreadsheet programs like Microsoft Excel® may be adequate. Commercial vendors also have products on the market to develop, track, and manage emissions inventory data.

parameter values, and any interim parameter values used in the calculations, may need to be tracked and managed in a way that allows one to quickly document new parameter values, and to ensure data integrity.

- **Summation of Multiple Emissions Records Reported for the Same Emission Source**: In some regulatory emissions databases, multiple sets of emissions from different processes are reported for the same source. This sometimes results in multiple emission rates of the same contaminant being reported from a single emission source (i.e., multiple emission records). For simplification in risk characterization, these multiple emission records (same contaminant at same source) are often summed before calculating the risk. If the total emissions from the facility result in high risk levels to a community, it may be necessary to revisit the original process-specific emissions when evaluating potential emissions reduction options.

#### 5.1.3.2 Verification and Correction of Source Locations

Source location data in existing inventories is sometimes reported by the facility and sometimes developed by a regulatory agency using a variety of surrogate information sources to fill data gaps. This can result in inventories that are variable in accuracy and format. Since incorrectly identifying the source location can have potentially significant impacts on risk results, it is important to verify the accuracy of the reported locations for each emission source.

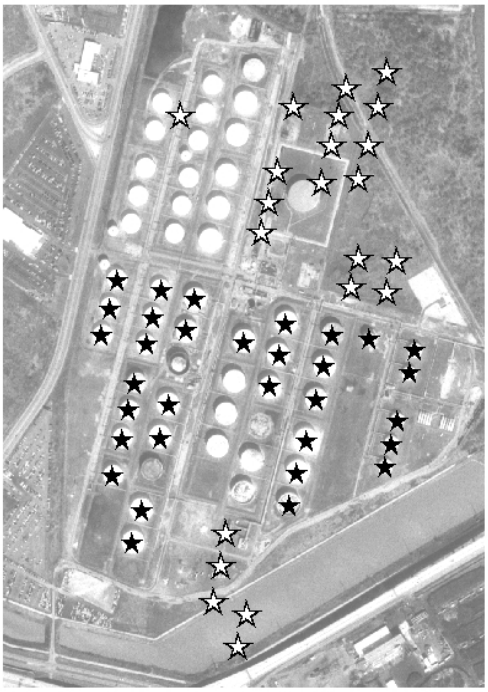
There are several tests that can be applied to source location information to verify its accuracy. One common approach (called a "geo-location process") is performed in two steps. First, source locations are adjusted to account for errors and inconsistencies in geographic position for each source that can result from using different geographic frames of reference, or "datums," when reporting locational coordinates. This can be accomplished by ensuring that all emission sources are reported in a common datum [e.g., 1983 North American Datum (NAD-83); see accompanying text box]. These positions are then graphically evaluated with respect to other known location information, such as facility boundaries, facility equipment and processing plants, land use zones, and other graphical data references.

An example of the geo-location method employed for multisource assessments is described below and shown graphically in Exhibit 5-5.

- **NAD 27 to NAD 83 Shift**: Each source location is reviewed to determine if the reported location was provided in NAD 83 or in NAD 27 format. For sources that are determined to have originally been reported in NAD 83, the reported source location is maintained in the project emissions inventory, and tracked as "not shifted" (this comment identifies the source location data as originally reported in NAD 83). For all other sources, the analyst assumes all locations are reported in NAD 27 and shifts the source locations reported in the emissions database to NAD 83 (e.g., the shift from NAD 27 to NAD 83 is approximately 200 feet north and 30 feet west for locations in south central United States). The shifted NAD 83 location becomes the source location for modeling, and is tracked as "shifted" without further comment. Both the reported and shifted source locations are then reviewed on a GIS platform and compared to referenced mapped data (see next bullet).

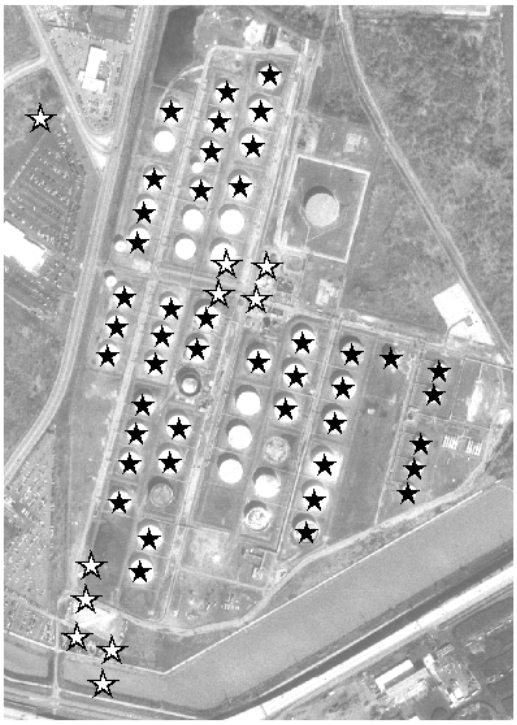
**Exhibit 5-5. Example of How to Geo-locate Sources**

**Before**



In this example, the analyst starts with an aerial photo of a facility of interest (a tank farm). The locations of the individual tanks are then plotted using the lat/long data from the existing inventory. In this example, some of the lat/long data (with locations represented by stars) are provided using the NAD83 datum and some are provided using the NAD27 datum. The unfilled stars are offset because they either are not the same datum as the photo, or the lat/long coordinates are incorrect for another reason.

**After**



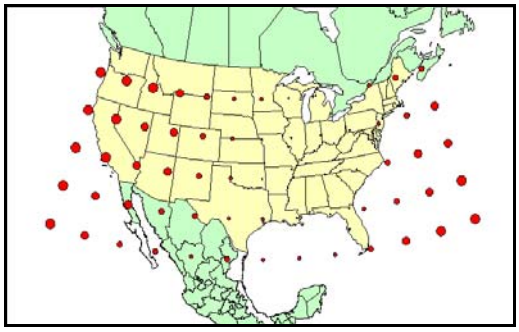
The lower picture shows the same site after the analyst converts the misplaced points from NAD27 to NAD83 and replots the locations of the tanks. It is clear that more of the tank locations now line up with the photograph. The analyst would need to further clarify the location of remaining questionable tank locations (indicated again with unfilled stars) based on additional data.

**North American Datum**

The earth is not a sphere but an ellipsoid distorted by rotation about its axis, with the globe bulging at the equator and flattened at the poles. There are multiple ellipsoid models that have been developed to approximate the shape of the earth; these different models are represented mathematically as datums.

For many years, the North American Datum of 1927 (NAD27) was the standard datum used in the United States. It is based on the Clarke ellipsoid of 1866, which was developed from a ground survey in Europe and North America in the 19th century. Use of this datum is gradually being replaced by the North American Datum of 1983 (NAD83) which is based on the World Geodetic System ellipsoid of 1984 (WGS84). Developed from satellite measurements of the earth surface in the 1970s and 1980s, NAD83 provides a more accurate representation of the earth's shape and a more accurate depiction of the location of objects on the earth.

Data sets should be presented in the same datum in order to be compared or used together. The coordinates generated for the same location using both NAD27 and NAD83 can differ by up to 200-300 feet in the western US to several tens of feet in the central and eastern US. The adjacent map indicates the difference between the two datums (the larger the dot, the more difference between coordinates).



There are several ways to convert between these two datums. Many desktop GIS software have conversion routines built in. The best conversion programs are based on the National Geodetic Survey's NADCON (North American Datum Conversion).

Source: USGS, *Datums and Projections: A Brief Guide*, March 1999. Available at: http://biology.usgs.gov/geotech/documents/datum.html.

Image used with permission from Tower Maps. Online at: http://www.towermaps.com/nad.htm.

- **GIS Review**: GIS review is then conducted by posting the reported and shifted source locations over background maps of high resolution aerial photographs [1-meter digital ortho quarter quad (DOQQ)], county boundary map, and digitized facility property boundaries. Analysts then look for remaining problems with source locations (e.g., an emission point in the middle of a lake). A GIS platform such as ESRI's ArcGIS software suite could be used for this review (http://www.esri.com/index.html). USGS DOQQ images as well as other geospatial data are available online for free or purchase from government and private sites, such as geodata.gov (http://www.geodata.gov/gos), the GIS Data Depot (http://data.geocomm.com), and other federal or state GIS web sites.[a]

[a] These software references and data sources are provided for information only; it is the analyst's responsibility to ensure the accuracy of data obtained from these or other sites.

In some cases, source location verification procedures may have been completed in the development of the emissions inventory (e.g., certain data augmentation and checking processes are completed for NEI data). However, a third step can also be completed to check those location coordinates for which default values have been assigned in the inventory used as a data source. For example, some sources in the NEI have been assigned default coordinates where actual source locations were not available. The default flags for such coordinates should be reviewed, and actual locations may need to be obtained as a part of the assessment.

#### 5.1.3.3 Chemical Speciation of Emissions

It is often the case that emissions are reported as pollutant mixtures, such as "gasoline," "volatile organic compounds," "hydrocarbons," or "particulate matter." This presents a problem for the assessment team, since the identity and amount of the various components in the mixture are needed because toxicity values are usually not created for such complex mixtures. To estimate identities and amounts of the mixture components, one would need to apply a ***speciation profile*** to the mixture. In general, speciation profiles are industry-specific or source category-specific conversion factors that are used to estimate pollutant-specific emission rates from emission rates of pollutant mixtures. For example, the toxic speciation profile for a particular type of gasoline might be one percent benzene, 10 percent toluene, and 5 percent xylene.

**Screening Chemical Mixtures**

If a speciation profile is not readily available for the source of interest, one screening-level technique that can be used to evaluate the importance of the mixture in the overall analysis of risk is to assume that the mixture is made up entirely of the most toxic constituent. For example, in a mixture containing compounds X, Y, and Z (but of unknown proportion), the analyst might assume (as a screening level exercise) that the entire mixture is made up of the most toxic chemical in the mixture (chemical X). If the risk posed by the mixture under this assumption is small compared to other sources and chemicals, the analyst may be able to drop it from further consideration (thus, averting the need for an accurate speciation profile for the mixture).

The most accurate way to determine the speciation profile is with analysis of the actual emissions source, but this is a very resource-intensive approach. Alternatively, if the emissions inventory contains speciated emissions for similar sources, the profile for those sources might be assumed to apply to the unspeciated sources. Similarly, speciation profiles for various source types are sometimes published in peer-reviewed journals. Industry-specific speciation profiles may be quite limited, but there is some information in EPA's AP-42 documentation for selected categories of sources (see http://www.epa.gov/ttn/chief/ap42/index.html). More information is available about speciation profiles of gasoline and onroad mobile source emissions in the MOBILE6.2 User's Guide (http://www.epa.gov/otaq/m6.htm).

#### 5.1.3.4 Spatial Allocation of Stationary Non-Point Source Emissions

In community-scale assessments, it is often necessary to obtain information about the exact location of all sources, when possible, rather than rely on "spatial surrogates" for diffuse, smaller nonpoint (see Section 3.2.2) sources that are reported in the aggregate in an existing emissions inventory. For example, the NATA risk characterization generally evaluates smaller sources that

are widely dispersed throughout urban areas (e.g., gas stations, dry cleaners, autobody shops, etc.) and reported in the aggregate by distributing the total amount of emissions from each such source category across a geographic area using a spatial surrogate (e.g., allocating dry cleaning emissions according to population) without consideration of the actual source locations. While this is appropriate in the NATA evaluation (given its intended purpose of providing a characterization of risk at the national scale), in a local-scale assessment, this detail may not provide the level of accuracy needed for local risk management.

**A Tip for Engaging the Community**

Refining the emissions inventory can take time and resources and people are sometimes tempted to take "short cuts" to avoid some of this work. However, keep in mind that a complete and accurate emissions inventory is the key to a successful multisource analysis.

One way to get the community involved in the process is to have them help refine the emissions inventory. With one short class in how to use a GPS, community members can be sent out to find and document the many small area sources in the study area. This easy process will help community members feel engaged, will teach them about the process, and will provide valuable information (basically for free) that can dramatically enhance the overall quality of the resulting emissions estimates.

For example, consider an emissions inventory that provides only one sum total tonnage of benzene emissions at the county level for gas stations. One way to allocate the emissions is by population (e.g., using census block data). While this puts the emissions where the people are (in a general sense), it is still only a guess about where the gas station emissions are actually occurring. To evaluate where the gas stations truly are in relation to the potentially exposed populations will require someone to physically locate the gas stations. This could be done by either a computerized search, a review of the phone book, or a "windshield survey" in which someone drives through the study area with a global positioning system (GPS) unit and physically records the exact location of each gas station.

Some tools exist to assist the analyst in allocation of non-point sources to specific locations. For example, EPA's Emissions Modeling System for Hazardous Air Pollutants (EMS-HAP) contains a processor that allows the analyst to model airport-related emissions (e.g., emissions from aircraft and aircraft refueling activities) as discrete sources located at airports instead of spatially-allocated mobile sources.

Sometimes it is neither necessary nor practical to gather this level of detail. Sometimes the contribution from a source type is so small that the effort to locate the individual emissions locations is not justified (see Appendix B for information on screening techniques for small, diffuse sources). In other cases, the resources may not be available to verify the locations and a more generic emissions allocation approach will be selected. Ultimately, the DQO's and resources available for the project will drive the efforts to identify the location of all the sources in a specific area. An example of one method for allocating diffuse source emissions across a geographic area is presented in Exhibit 5-6; more detailed information is described in the *How To Manual*,[1] the NATA risk characterization documentation (http://www.epa.gov/ttn/atw/nata/), and the NEI documentation (http://www.epa.gov/ttn/chief/net).

#### 5.1.3.5 Mobile Sources

For the purposes of inventory development, the choice of conducting a top-down versus a bottom-up inventory for mobile source emissions is based on the purpose and scale of the inventory application as well as available data. For a community-scale assessment, it is preferable to use data specific to the area of study, as this will provide more accurate data regarding the sources and distribution of risk in the population.

Top-down inventories are developed for use in national- or regional-scale assessments (where highly refined data is impractical), such as the NEI. To estimate mobile source emissions the NEI uses various surrogates such as population and vehicle activity data and equipment activity data to allocate emissions to individual counties. County-level emissions are then allocated to smaller geographic areas (grid cells or census tracts) using spatial allocation factors such as land use or roadway miles.

County-level emissions for on-road sources are estimated as the product of emission factors (grams per mile) and vehicle miles traveled (VMT), by vehicle class, roadway type, and month or season. County-level VMT in the NEI is allocated from state or urban area totals obtained from the Federal Highway Administration's Highway Statistics series using county level population data. County level emissions are then computed using a highway vehicle emissions factors calculated using EPA's MOBILE6.2 model. For national and regional scale analysis, default or average values are often used for many input parameters such as driving speed and vehicle age distribution. These emissions are then spatially allocated to the subcounty level for air quality modeling using an emissions preprocessor such as EMS-HAP.[(b)] EMS-HAP allocates on-road emissions using road miles for different road types. Emissions are also allocated temporally, by hour of the day, using this preprocessor and time-activity profiles.

County-level emission inventories for nonroad sources are estimated using the NONROAD model (see http://www.epa.gov/otaq/nonrdmdl.htm). Allocation factors used to calculate emission inventories for nonroad equipment can be found in the EPA Technical Report No. EPA420-P-04-014 and allocation factors for aircraft, commercial marine vessels and locomotives can be found at http://www.epa.gov/ttn/chief/net.

National Mobile Inventory Model (NMIM) is a free, desktop computer application developed by EPA to calculate estimates of current and future emission inventories for on-road motor vehicles and nonroad equipment (see http://www.epa.gov/otaq/nmim.htm). NMIM uses MOBILE6.2 and NONROAD to calculate emission inventories, based on multiple input scenarios that the user enters into the system. NMIM can be used to calculate national, individual state, or county inventories.

Inventory estimates derived using the top-down approach are very useful as screening tools and for identifying priorities for further analysis. However, surrogates may not adequately represent local mobile source activity and default inputs used in emission models may not reflect local-scale conditions. Since studies have demonstrated that there can be strong spatial gradients of some pollutants associated with roads, more accurate emissions data at the local scale is important in developing strategies to assess and reduce risk at the local level.

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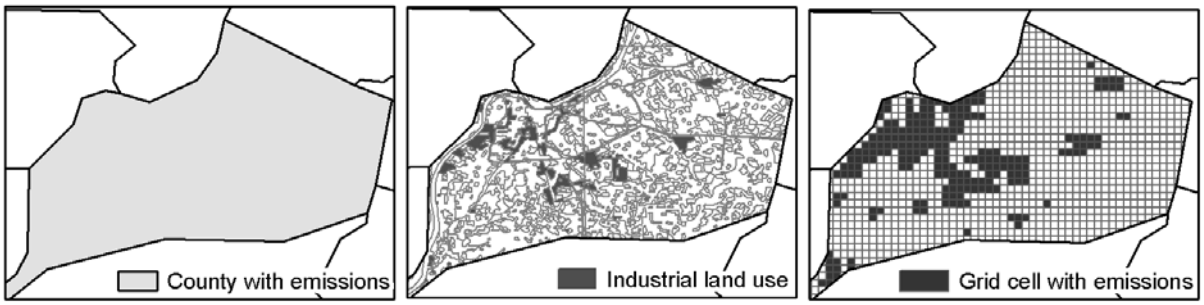
[b] For more information on EMS-HAP see www.epa.gov/scram001/tt22.htm.

A bottom-up method to develop mobile source emissions inventories uses local-scale input data specific to the community being studied. To develop a local-scale inventory for on-road mobile sources, emissions are assigned to individual roads and a Travel Demand Model (TDM) provides data specific to the roadways (see Exhibit 5-6). Models employing individual roadway data are termed 'link level' models. Information provided by a TDM includes roadway traffic volume,

**Exhibit 5-6. Examples of Spatial Allocation of Emissions**

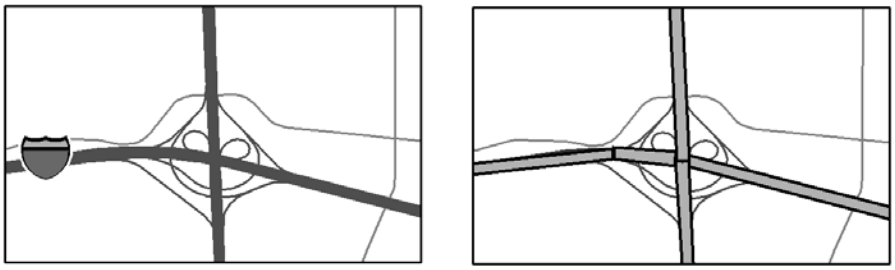



1. Gather data on area source emissions from a database such as NEI for a location (e.g., a county).

2. Use a spatial surrogate (e.g., industrial land use) to identify locations where area source emissions would occur.

3. Spatially allocate the area source emissions to small grid cells that overlap areas classified with the surrogate land use. Divide the county's emissions among the selected cells.

**Spatial allocation of diffuse stationary point sources:** In this example, county-level emissions data for a given type of emission source are assigned to smaller cells using land-use data and GIS techniques. Although this procedure is not as accurate as determining actual source locations, it offers a refinement to the county-level emission estimate that may be appropriate in some cases (e.g., considering the resources and desired level of detail of the assessment). The assignment of source locations to grid cells would be particularly useful when using a grid-based model.



1. Gather data for on-road mobile sources based on road type and usage in the area of interest.

2. Apply the emissions to road segments based on length and other properties of each road. Create area or volume sources to represent the on-road emissions in a model.

**Spatial allocation of mobile sources:** In this example, emissions from vehicles on a well-traveled road are estimated based on available information and then assigned to area or volume sources for inclusion in dispersion modeling.

capacity, number of lanes, and sometimes speeds. These data can be used with the MOBILE6.2 emissions model to create detailed emissions concentrations and spatial distributions.[c] For nonroad emissions, use of local equipment population and activity data can greatly improve the quality of inventories for local scale assessments. Applying a bottom-up inventory in a dispersion model for local-scale assessments has several advantages over top-down approaches, including the ability to identify communities with potentially higher risks, better characterization of pollutant gradients and improved temporal resolution.

To estimate ambient concentrations for community-scale mobile source assessments, air dispersion models are used, as discussed in the following section. For mobile source applications, dispersion models such as ISC or AERMOD can be used, and are especially useful in cases where a freight terminal, port or similar facility is being modeled. Models designed more specifically to estimate ambient concentrations of mobile source emissions include Gaussian plume models for line sources such as CALINE3 (to model episodic events) and CALINE4 (to model annual averages). CAL3QHC is the EPA-approved model for assessing intersections that is includes traffic queues, idling and stop/go cycles. More information regarding mobile source emission models can be found at www.epa.gov/otaq/models.htm. Information on air quality models can be found on the SCRAM website (www.epa.gov/scram001).

## 5.2 Air Dispersion Modeling

Air dispersion modeling is used in the multisource analysis to simulate the transport of chemicals released from a source through the air to a point where a person can inhale them. The process is performed using a computer with the resulting concentrations being represented at various points (referred to as modeling locations or nodes, also known as receptor locations or nodes), usually an evenly spaced grid located around the source out to a predetermined distance. ATRA Volume 1, Chapter 9, provides an overview of air dispersion modeling used in air toxics risk assessments, including examples of air dispersion models and air dispersion model applications. Documentation, software, and user's guides for commonly-used air dispersion models are available on EPA's SCRAM website (http://www.epa.gov/ttn/scram/). Several EPA guidance documents related to modeling air toxics are also listed in the text box below.

[c] See http://www.planning.dot.gov/Documents/BriefingBook/BBook.htm#2BB for additional information on the Metropolitan Transportation Planning Process.

**Selected EPA Guidance on Air Quality Modeling of Air Toxics**

EPA's Air Quality Modeling Group has developed numerous guidance documents on modeling air toxics pollutants that may be useful for reference. Below is a list of some of these documents.

- *User's Guide to TSCREEN, A Model For Screening Toxic Pollutant Concentrations.* 1990.
- *Guidance for Application Of Refined Dispersion Models For Air Toxics Releases.* 1991. EPA-450/4-91-007.
- *Evaluation of Dense Gas Simulation Models.* 1991. EPA-450/4-90-018.
- *Workbook of Screening Techniques for Assessing Impacts of Toxic Air Pollutants (Revised).* 1992. EPA-454/R-92-024.
- *Guidance on the Application of Refined Dispersion Models for Hazardous/Toxic Air Releases.* 1993. EPA-454/R-93-002.
- *Contingency Analysis Modeling for Superfund Sites and Other Sources.* 1993. EPA-454/R93-001.
- *User's Guide to TSCREEN- A Model for Screening Toxic Air Pollutant Concentrations (Revised).* 1994. http://www.epa.gov/scram001/userg/screen/tscreend.pdf.
- *Development and Testing of a Dry Deposition Algorithm (Revised).* 1994. EPA-454/R-94-015.
- *Air/Superfund National Technical Guidance Study Series, Volume V-Procedures for Air Dispersion Modeling at Superfund Sites.* 1995. EPA-454/R-95-003. http://www.epa.gov/scram001/guidance_other.htm
- *Dispersion Modeling of Toxic Pollutants in Urban Areas: Guidance, Methodology and Applications.* 1999. EPA-454/R-99-021. Office of Air Quality Planning and Standards, Research Triangle Park, NC. http://www.epa.gov/scram001/guidance_other.htm
- *A Simplified Approach for Estimating Secondary Production of Hazardous Air Pollutants (HAPs) Using the OZIPR Model.* 1999. http://www.epa.gov/scram001/guidance/reports/oziprpt/oziprhps.pdf.
- *User's Guide for the Assessment System for Population Exposure Nationwide (ASPEN, Version 1.1) Model.* 2000. http://www.epa.gov/scram001/userg/other/aspenug.pdf.
- *Example Application of Modeling Toxic Air Pollutants in Urban Areas.* 2002. http://www.epa.gov/otaq/toxics.htm.
- *User's Guide for the Emissions Modeling System for Hazardous Air Pollutants (EMS-HAP) Version 3.0.* 2004. http://www.epa.gov/scram001/userg/other/emshapv3ug.pdf.
- *Guidance on Hazardous/Toxic Air Releases* (5 documents). http://www.epa.gov/scram001/guidance_other.htm.
- *National Speciality Workshop on Technical Tools for Air Toxics Assessment Final Report.* 1997 http://www.epa.gov/scram001/guidance_other.htm.

This section focuses on information for selecting and applying an air dispersion model in a multisource community-scale assessment. A detailed example of the application of the ISCST3 model for multisource community-level air toxics analysis is provided in an abbreviated version in Appendix A. As emphasized throughout this chapter, other air modeling techniques (e.g., using more refined models that take into account chemical transformation) may also be appropriate, depending on the desired level of detail and the resources available to the analyst. For example, the use of a unit emission rate in air dispersion modeling is described in this chapter. This step may incur a small "cost" in accuracy that may be acceptable given the approach's efficiency and flexibility when compared against the time and resources it could take to perform an alternate analysis (see Section 5.2.3.2 and the text box in that section for more details).

### 5.2.1 Air Dispersion Modeling DQOs

Prior to selecting or running an air dispersion model, the partnership team must agree to study-specific modeling input parameter DQOs (example DQOs are provided below).

- **Accuracy**: Point source emission locations accurate to within some acceptable distance (e.g., 100 meters);
- **Completeness**: All sources emitting at least X tons/year of the compound within some acceptable distance of the study area boundary (e.g., 1 mile);
- **Completeness:** Stack parameters provided for all point sources;
- **Level of detail:** Emission sources stratified by Standard Classification Code (SCC) and AIRS area and mobile system (AMS) codes;
- **Level of detail:** Spatial resolution of model nodes to some acceptable geographic subdivisions (e.g., 90 meter spacing);
- **Level of detail**: Spatial resolution of non-point source emission to some acceptable geographic subdivisions (e.g., US Census tracts, 2-km grid squares).

Note that many of the dispersion model DQOs link directly to the quality of the emissions inventory and the accuracy of the model inputs. Understanding how the selected air model works, the questions to be answered, and the various resolutions of air model input parameters are key to understanding the accuracy of the dispersion results.

### 5.2.2 Air Dispersion Model Selection

Criteria for selection of an air dispersion model for a cumulative multisource assessment include (1) the ability to meet the modeling DQOs, and (2) the availability of required data inputs. Timing considerations are also important because some modeling approaches are dramatically more time intensive than others (which can lead to higher costs).

#### 5.2.2.1 Available Models

Available air dispersion models range from those that are relatively easy to use with existing inventory data to complex models with additional input requirements. In addition, the physical characteristics of the study area may influence the model selection since some models are better at estimating concentrations in complex terrain (e.g., in river valleys, coastal environments). ATRA Volume 1, Chapter 9, provides an overview of the various types of models, their capabilities, and their utility in different types of settings. Typical applications are summarized in Exhibit 5-7 (this information is updated from that originally presented in Exhibit 9-5 in ATRA Volume 1, Chapter 9). For multisource assessments, the last two columns of Exhibit 5-7 (i.e., multiple sources) are most relevant.

**Exhibit 5-7. Typical Applications for Common Dispersion Models**

| | Averaging Period | Terrain Type | Single Source | | Multiple Sources | |
|---|---|---|---|---|---|---|
| | | | Rural | Urban | Rural | Urban |
| Screening Models | Short Term (1-24 hour average) | Simple | SCREEN3 | SCREEN3 | ISCST3, AERMOD | ISCST3, AERMOD |
| | | Complex | SCREEN3, ISCST3 | SCREEN3, ISCST3 | ISCST3 | ISCST3 |
| | Long Term (Monthly-Annual) | Simple | ISCLT3 | ISCLT3 | ISCLT3, ASPEN | ISCLT3, ASPEN |
| | | Complex | ISCST3 | ISCST3 | ISCST3 | ISCST3 |
| Refined Models | Short Term (1-24 hour average) | Simple | ISCST3, AERMOD | ISCST3, AERMOD | ISCST3, AERMOD | ISCST3, AERMOD, CMAQ-AT |
| | | Complex | AERMOD, CALPUFF | AERMOD, CALPUFF | AERMOD, CALPUFF | AERMOD, CMAQ-AT, CALPUFF |
| | Long Term (Monthly-Annual) | Simple | ISCST3, AERMOD | ISCST3, AERMOD | ISCST3, AERMOD | ISCST3, CMAQ-AT, AERMOD |
| | | Complex | CALPUFF, AERMOD | CALPUFF, AERMOD | CALPUFF, AERMOD | CALPUFF, CMAQ-AT, AERMOD |

#### 5.2.2.2 Ability to Meet DQOs

ATRA Volume 1, Chapter 9, also provides discussion of some of the strengths and weaknesses of each model. Review of this information will be helpful in determining which of the commonly used air dispersion models have the ability to meet the DQOs for a specific multisource assessment, such as the capability to treat complex terrain, perform dry and wet deposition, assess chemical transformation, and evaluate building downwash.

For example, ISCST3 is one of the regulatory air dispersion models that has been used most commonly by regional, state, and local agencies. Because the ISCST3 model accomplishes all of the same modeling objectives with more universal application to various sources types than ISCLT3, and because ISCST3 provides short-term (e.g., 1-hour) concentration estimates, ISCST3 is the air dispersion model that has been used for many community-scale assessments (particularly those that focused on both long- and short-term impact assessment).[(d)]

It is important to note that AERMOD has replaced ISC as the preferred regulatory model for EPA air dispersion modeling applications. The rule establishing AERMOD as the preferred model became effective December 9, 2005, and analysts are encouraged to use AERMOD rather than ISC3 for dispersion modeling applications due to the superior ability of AERMOD to estimate ambient air concentrations resulting from air emissions, especially in modeling downwash and dispersion across complex terrain. EPA has stated that the use of ISC3 for regulatory modeling analyses will be allowed during the one-year period following December 2005 at the discretion of the regulatory authority for which the analyses are being conducted. Technical documentation, user guidance, and other materials related to AERMOD (including detailed comparisons of AERMOD to ISCST3 and other dispersion models) are available from EPA's Support Center for Regulatory Atmospheric Modeling at http://www.epa.gov/scram001/dispersion_prefrec.htm#aermod.

**A Note on the Use of AERMOD for Community-Scale Assessment**

Because many community-scale assessments conducted to date have used ISC3, and because ISC3 (specifically, ISCST3) is the current modeling platform used in the RAIMI methodology, ISC is referenced in some of the examples presented in this chapter. However, the analyst should be aware that a new dispersion model called AERMOD (American Meteorological Society/EPA Regulatory Model) recently replaced ISC3 as the EPA's preferred model for certain regulatory applications (see http://www.epa.gov/scram001/dispersion_prefrec.htm#aermod) and analysts should consider using this model, when appropriate. (Note that the RAIMI methodology may be updated in the future to provide the same automated features using AERMOD as it currently does with ISCST3. Analysts should check the RAIMI website for updates to the RAIMI software – see http://www.epa.gov/Arkansas/6pd/rcra_c/raimi/raimi.htm.)

[d] It should be noted that while achieving certain community-level modeling DQOs with respect to the temporal resolution may be limited if ISCLT3 is selected (e.g., because it can provide only annual average concentration predictions), some commonly used air toxics modeling applications (e.g., HEM-Screen) use ISCLT3 as part of their architecture. Analysts are again reminded to pick the analytical tool that will match the DQOs for the study at hand.

**Automating the Process - Preparing Input Data**

Air modeling for cumulative multisource assessment must consider a variety of issues, including the local variability in land use, terrain, and meteorological conditions to address site-specific fate and transport of airborne contaminants. Processing large data files of emissions data, meteorological data, land use, and terrain information is time- and computer-intensive, particularly when assessing releases from hundreds or thousands of sources and several computer tools have been developed to help bring efficiency to the process. Additionally, automation of methods helps ensure more consistency and fewer errors in the air modeling analyses. Some of the available air modeling data preprocessors include:

**The RAIMI Air Modeling Preprocessor**. The RAIMI Air Modeling Preprocessor (AMP) provides automated data pre-processing to prepare source-specific meteorological and air model source input files while accounting for localized variations in site characteristics, including variations in land use and terrain (see http://www.epa.gov/Arkansas/6pd/rcra_c/raimi/raimi.htm).

**Emissions Modeling System for Hazardous Air Pollutants (EMS-HAP).** This SAS-based processor can prepare annual emission inventory data from a source like NEI for subsequent air quality modeling using, for example, the ASPEN or ISCST3 model (see http://www.epa.gov/ttn/chief/emch/projection/emshap30.html).

**Sparse Matrix Operator Kernel Emissions (SMOKE).** This processor speciates and temporally and spatially allocates mass emissions inventory data and prepares data in formats for input to emission estimation tools such as MOBILE6 and BEIS3 (see http://cf.unc.edu/cep/empd/products/smoke/index.cfm#Summary).

Other factors or circumstances may also be important in selecting an appropriate model that can meet the DQOs of an assessment. Two examples of such factors are presented here; other considerations may also be important.

- **Treatment of meteorological data.** In localized areas with complex wind patterns, consideration of a model's treatment of meteorological data is important. The most accurate results for these localized wind patterns will be obtained with a model like CALPUFF that uses 3-dimensional wind fields. However, the development of such wind fields requires the application of a meteorological model and assimilation of multiple raw measured data sets which can become quite resource-intensive (see http://www.epa.gov/scram001/tt22.htm#calpuff).

- **Spatial resolution and formation of secondary pollutants.** Achievement of modeling DQOs with respect to the spatial resolution of model predictions may be limited if a numerical grid model (e.g., CMAQ-AT) is selected, since the resolution is constrained to the size of the three-dimensional grid cells throughout which pollutant concentrations are assumed to be uniform. However, the upside is that these types of models can be used to address the formation of secondary pollutants. In cases where secondary pollutants are of interest, the ability to model the formation of such pollutants using a grid model may be more important than the higher spatial resolution afforded by a Gaussian plume model.

#### 5.2.2.3 Availability of Required Model Inputs

Depending on the air quality model, a variety of inputs will be required. As the model becomes more complex, the data needs also tend to increase. In addition, some models will allow the user to select preset defaults for various inputs or provide user-specified data. Which course the user selects, of course, links back to the DQOs for the modeling exercise, and to the needs and purpose for the assessment as developed during the planning process.

For the purpose of cumulative multisource assessment, the air dispersion model will generally require, at a minimum, the following inputs:

- ***The Emissions Inventory***. It is worth restating that problems with the emissions inventory must be addressed prior to dispersion modeling to obtain useful results, no matter which model is selected. For example, many air toxics emissions can display a strong concentration gradient once released to the atmosphere. Thus, a mislocated source in the emissions inventory can also pose a critical accuracy issue in the resulting air modeling results.

  Note that with the exception of emissions resulting from operational upsets or maintenance activities, emissions are usually reported as annual totals. Some additional data augmentation may be required to ensure that source-specific temporal profiles correspond to the type of exposure being assessed (i.e., chronic or acute).

- ***Speciation Profiles***. As discussed above, emissions are sometimes reported as groups of compounds in some state inventories (e.g., gasoline, volatile organic compounds, or particulate matter). To develop chemical-specific estimates of ambient concentration in the dispersion modeling exercise, speciation profiles specifying the fractional composition of the emission (e.g., 5% benzene, 10% toluene, 5% xylene) will be needed.

- ***Meteorological Data***. Selection of appropriate meteorological data is critical for any air modeling project. In many situations, data collected at the nearest Nation Weather Service (NWS) station is adequately representative. However, in some situations (e.g., severely complex terrain such as a source located in a deep river valley) meteorological data from the nearest NWS station may not be representative of the actual conditions. For these more complex situations, it is recommended that the analyst consult with the appropriate EPA regional or state Agency modeling contact for assistance in selecting the most appropriate data. A list of EPA regional and state Agency modeling contacts is provided on EPA's SCRAM website (http://www.epa.gov/scram001/tt28.htm). Additional guidance for preparation of meteorological data for use with Gaussian models is also available on EPA's SCRAM website (http://www.epa.gov/scram001/tt24.htm). The development of 3-dimensional wind fields for more advanced models like CALPUFF and UAM-Tox require the use of a meteorological model, a resource-intensive process. However, the models used for geographic areas that are out of compliance with the tropospheric (ground-level) ozone NAAQS also use 3-dimensional wind fields, so that for such areas at least some of the requisite meteorological data may already be available.

- ***Secondary Pollutants***. When the analysis needs to evaluate the production of secondary pollutants, the input to the model will need to include emissions of precursor compounds. The precursors for many of the secondary air toxics are generally contained in emission

inventories developed for modeling tropospheric ozone, which is also a secondary pollutant. For such areas a precursor inventory that can be used to model secondary air toxics of interest may be available. Examples of secondary pollutants and the emitted pollutants from which they are formed are provided in the accompanying text box. A technical discussion of the formation of secondary pollutants is provided in ATRA Volume 1, Chapter 8.

### 5.2.3 Special Considerations

When performing a multisource assessment, there are several special considerations that should be noted. Some of these flow from the need to meet study-specific DQOs; others relate to the computational requirements of evaluating and tracking a large array of chemicals and release points. Several special considerations that commonly occur are emissions partitioning, the use of unit emissions rates, working with a "universal grid," bounding analyses for non-point sources, and dealing with background concentrations; other considerations may also need to be addressed depending on the model and technical approach implemented.

#### 5.2.3.1 Emissions Partitioning

To account for the partitioning of emitted contaminants among various physical phases in the ambient air after release in both Gaussian and puff models, it is important to consider the need to conduct separate air modeling runs to represent partitioning to the vapor phase, particle phase, and particle-bound phase. Partitioning of emitted contaminants is of particular concern when a contaminant is released as a particle, or has a portion of its mass adhered onto particles because the fate of emitted pollutant mass can be sensitive to the deposition and removal processes.

The tendency of a contaminant to be present in a particular phase (i.e., as a vapor, as a particle, or adsorbed onto existing particles) can be expressed as the fraction of the air concentration of the contaminant in the vapor phase, $F_v$, as follows:

- All contaminant in the vapor phase: $F_v = 1.0$
- Some contaminant in the particle-bound phase: $0 < F_v < 1.0$
- All contaminant in the particle phase: $F_v = 0$

The vapor phase is used to evaluate volatile organic compounds (VOCs) that are assumed to occur in the vapor phase (i.e., contaminants with $F_v = 1.0$).

The particle-bound phase is modeled to evaluate the fraction of organic contaminants that upon release to the atmosphere have condensed onto the surface of associated particles (i.e., contaminants with $F_v$ between 0 and 1.0). The portion of contaminants in the particle-bound phase is dependent on the particle surface area available for chemical adsorption.

The particle phase is modeled when evaluating metals and organic contaminants with low volatility that are assumed to occur in the particle phase (i.e., contaminants with $F_v = 0$). Particle size is the main determinant of the dispersion and deposition of particles in the emission, whether wet or dry deposition.

**Processes that Alter Atmospheric Concentrations of Chemicals**

A variety of physical and chemical processes can affect the fate and transport of toxic pollutants in the atmosphere. For example, dry and wet deposition reduce atmospheric pollutant concentrations in the absence or presence of precipitation, respectively. Another mechanism for pollutant removal is by chemical reactions in which a toxic air pollutant is destroyed through the action of sunlight, through reactions with atmospheric chemical pollutants, or through a combination of these pathways. Yet another possibility is for potentially harmful pollutants to be formed as a result of atmospheric chemical reactions (a process that is called secondary production or secondary formation - see examples below). Analysts are encouraged to understand the capabilities of the various fate and transport models to account for chemical removal and formation and to carefully articulate the uncertainties in the resulting concentration estimates based on the tools selected for a given assessment. (A more thorough discussion of fate of air toxics in the atmosphere is provided in ATRA Volume 1, Section 8.3.)

**Examples of Secondary Pollutants**

| Secondary Pollutant | Formed From |
|---|---|
| acetaldehyde | propene, 2-butene |
| acrolein | 1,3-butadiene |
| carbonyl sulfide | carbon disulfide |
| o-cresol | toluene |
| formaldehyde | ethene, propene |
| hydrogen chloride | nitric acid, chlorinated organics |
| methylethyl ketone | butane, branched alkenes |
| N–nitroso-N–methylurea | N–methylurea |
| N–nitrosodiethylamine | dimethylamine |
| N–nitrosomorpholine | morpholine |
| phosgene | chlorinated solvents |
| propionaldehyde | 1-butene |

Source: Rosenbaum, A.S., Ligocki, M.P., and Wei, Y.H. 1998. Modeling Cumulative Outdoor Concentrations of Hazardous Air Pollutants, Volume 1: Text. SYSAPP-99-96/33r2. Prepared for U.S. EPA, Office of Policy, Planning and Evaluation, by Systems Applications International, Inc., San Rafael, CA. 1998.

A detailed example of the treatment of emissions partitioning in air dispersion modeling is presented in EPA's *Regional Air Impact Modeling Initiative (RAIMI): Standard Screen Analysis Methods, Technical Support Document,* (see http://www.epa.gov/earth1r6/6pd/rcra_c/raimi/raimi.htm). For more information on this and other related subjects, consult the *Guideline on Air Quality Models* (GAQM)[2] on EPA's Support Center for Regulatory Air Models (SCRAM) website (http://www.epa.gov/scram001/index.htm). Guidance materials for the specific models discussed here (e.g., ISCST3, AERMOD, CALPUFF) can also be found on this site.

#### 5.2.3.2 Unit Emission Rates

In standard Gaussian plume models (e.g., ISCST3, AERMOD) and puff models (e.g., CALPUFF), concentration predictions resulting from a release are proportional to the emission rate. That is, for a given set of stack parameters and meteorological conditions, the concentration predicted for an emission rate of 2 g/s would be twice as high as the concentration predicted for an emission rate of 1 g/s.

This relationship can be used to minimize computer resources when modeling an emission source that releases more than one pollutant, or if multiple emission rate scenarios need to be evaluated (e.g., reported actual emissions, permitted allowable emissions, revised quantities of emissions due to operational changes, or inclusion of new contaminants in the emissions profile). Instead of estimating receptor concentrations several times, once for each pollutant or scenario, the modeler can estimate concentrations at each grid node receptor for an emission rate of 1 unit, and then scale the receptor concentration prediction by the pollutant emission rate with a post-processor to determine the corresponding prediction for each pollutant. Ultimately, the user need only provide the actual emission rates for each source. Then, as a post-processing step, emission rate scalars are applied to each receptor/source combination, and the concentration contribution from each source is summed for each grid node receptor/pollutant combination.

**Use of Simplifying Assumptions – A Balancing Act**

Simplifying assumptions – such as the use of a unit emission rate – are sometimes employed to allow for a more efficient assessment. However, the analyst must be aware of the impact of assumptions on the end results (i.e., are they likely to over or underestimate exposures and risks). Overall, it is the planning and scoping team's responsibility to balance the needs of the assessment (embodied by the modeling DQOs) and the desired level of detail with the resources available to complete the assessment. Since some of the people on the planning and scoping team will have little experience in this area, technicians familiar with these issues will need to carefully describe the various options so that the overall planning effort will result in a plan that meets the needs of all team members.

For example, suppose that a particular stack A emits benzene at a rate of 3 g/s and toluene at a rate of 5 g/s. Furthermore, suppose that the Gaussian model predicts a grid node receptor concentration of 0.4 $\mu g/m^3$ for an emission rate of 1g/s from stack A. With a post-processor, the modeler can scale the predicted receptor concentration to obtain a benzene concentration of 1.2 $\mu g/m^3$ and a toluene concentration of 2.0 $\mu g/m^3$. (This type of relationship is applied in the RAIMI methods using the ISCST3 model.)

In addition to eliminating the extensive effort that would be required to model each pollutant separately, the benefit of this approach is that it provides the flexibility of being able to conduct "what if" scenarios using any combination of new or revised emissions scenarios without having to conduct additional air dispersion modeling of the source. Thus, the same modeling for a source can be used to evaluate that source's potential resulting risks for any combination of emissions scenarios specific to current or anticipated future releases. (Being able to perform such "what if" scenarios would be important for a community that is evaluating both risk mitigation options for current emissions as well as looking at the potential impact of growth in the future.)

Note that proceeding in this manner is not without its limitations. For example, such simplifying assumptions have the tendency to treat all chemicals in a group as equal (e.g., all VOCs behave the same) and does not take into account the different fate and transport characteristics of chemicals once released to the environment. If a more robust analysis of individual constituents is needed, analysts may need to take a different (and likely more computationally challenging) approach. A list of pros and cons of using the unit emission rate approach is provided in the accompanying text box.

#### 5.2.3.3 Using a Universal Grid

Because of the need to integrate several types of geographic information (e.g., location of sources, population data, digital elevation data, land use) for a multisource modeling analysis, defining a "universal grid" system for the entire project provides increased efficiency. The "universal grid" system selected should be a standardized geographic coordinate system consistent to all geographic-based data. A convenient choice is the NAD 83 latitude/longitude curvilinear (datums such as NAD83 are discussed in Section 5.1.3.2), which provides this consistency and efficiency since it is the system that is used by the U.S. Geological Survey (USGS) for land use/land cover, digital terrain, aerial photographs and feature maps (http://biology.usgs.gov/geotech/documents.html). Because the latitude/longitude system is not limited in spatial extent, it also allows for seamlessly tracking source locations and integrating air model and risk characterization results over distances greater than ten kilometers, typical of community scale analyses. However, distances and areas cannot be measured accurately in a latitude/longitude system. An alternative choice would be the Universal Transverse Mercator (UTM) system (http://erg.usgs.gov/isb/pubs/factsheets/fs07701.html) used by most air dispersion models [the UTM system is rectilinear (as opposed to the curvilinear system), which therefore limits the size of the modeling region to some extent, but provides accurate area and distance measurements within the modeling region]. For the air modeling portion of community scale risk assessments, some air models require temporary conversion of latitude/longitude coordinates into a rectilinear system to satisfy the mathematical assumption in the air model. For example, RAIMI utilizes the UTM system to satisfy this computational requirement of the ISCST3 air model before converting the air model results at grid nodes back into the Universal Grid system. This integrated universal grid approach, as implemented in the RAIMI methodology, further supports special spatial processing capabilities, such as risk averaging across and between grid nodes (i.e., RAIMI approach for determining average exposure concentration or risk values for census blocks).

Once a coordinate system is selected, it can be used to define a reference set of locations that span the modeling region in the form of a grid. Required geographic-based data, such as terrain elevations and land use/land cover, are specified for each grid node. These grids nodes may also be used to define the modeling receptors, or the grid cell centroids for a numerical grid model to avoid the necessity for data interpolation.

**Automating the Process: The RAIMI ISCBatch and Air2GIS**

**ISCBatch** allows the user to execute several ISCST3 air modeling runs in a single "batch run." For each run that is completed as a part of this "batch," the air model generates results for each grid node (approximately 7,500-8,000 nodes) including a discrete value for the one-hour average air concentration for use in acute risk assessment, and annual average values for air concentration, dry deposition, and wet deposition for use in chronic risk assessment.

**AIR2GIS** is a software tool that assembles the ISCST3 modeling output files for each modeled source and creates a single file for import into the Risk Management Analysis Platform (Risk-MAP; discussed in Chapter 6). This allows the user to track results for each source and grid node location using Risk-MAP.

For more information on the RAIMI ISCBatch and Air2GIS, see: http://www.epa.gov/earth1r6/6pd/rcra_c/raimi/raimi.htm.

### 5.2.4 Dealing with Background Concentrations

An important consideration for both the understanding of study area cumulative risk and for the evaluation of model performance is the ***background concentration*** of toxic chemicals in study area air. The term background concentration is used here to mean the ambient pollutant concentration that would occur in the study area in the absence of the emission sources being explicitly evaluated in the air dispersion modeling effort. Example components of background concentrations may include (1) local emission sources not included in the model inputs, (2) emissions transported from sources outside of the modeling domain, including those immediately upwind of the study area and those more distant, and (3) historical releases of persistent compounds.

**The Importance of Background Concentrations**

Depending on the circumstances, the background concentration of a chemical in an area may be trivial compared to the influence of local emissions sources or it may dwarf the local sources (potentially making the estimated risk using only the local inventory of source substantially different from the cumulative risk from air toxics actually present). Likewise, the air dispersion model predictions of ambient concentration based on only local emission sources may be difficult to compare with measured concentrations since measured concentrations capture all sources influencing the monitor, including background sources. The planning and scoping team should keep this in mind as they develop their analysis plan in order to allow for the development of an appropriate level of understanding of potential background concentrations.

The first component can be addressed by creating as comprehensive a local emission inventory as possible. There are several approaches for addressing the second component, (i.e., medium- and long-range transport). One way is to estimate the value of this component from upwind measurements, if available. However, this approach can be difficult to interpret if there are several dominant wind directions for the modeling region. An alternative approach is to estimate the value on the basis of model predictions. Still another approach is to expand the modeling domain to include all significant medium- to long-range emission sources, if possible. Regarding the third component, upwind measurements or estimates of regional background concentration may be available from the

**Using a Unit Emission Rate: Pros and Cons**

Use of a unit emission rate in air dispersion models offers advantages in terms of flexibility and efficiency, but also potential drawbacks with respect to accuracy and data management. A few of the key pros and cons are summarized here.

**Pros:**

- Emissions tracking is maintained in a separate database by emissions specialists, which helps minimize the need to repeat air modeling. For example, if a stack location is incorrectly reported in an emissions inventory for one source, only that source will need to be modeled again, rather than re-modeling all sources.

- Automated generation of air model input files is simplified by not tracking and integrating emissions databases.

- Air modeling can proceed with source parameters while emissions data inventories are assembled and verified in parallel, rather than sequentially. Thus, the project performance schedule and expertise are managed in parallel, accelerating project schedules and allowing functional performance to be completed by specialists in their disciplines.

- For sources run at unit emission rates, separate air model runs can be performed to account for the different reaction rates in the atmosphere of various chemicals emitted. For example, if the source emits both high and low reactivity chemicals, two separate air model runs with appropriate reaction rates for that source will account for the chemical transformation. The emission rate for the highly reactive chemical is multiplied by the air parameter results from the highly reactive run, and the emission rate for the low reactivity chemicals is multiplied by the results from the low reactivity run.

**Cons:**

- Air modeling of individual sources requires data management during execution as well as results tracking for integration with emissions data as a post-processing step.

- File management is more complex compared to traditional air modeling, where all sources are compiled at specified emission rates into large single runs.

- When air modeling at 1 g/s for all sources, if a source has very low impacts (i.e., tall stacks impacting grid nodes long distances from release) the source impacts will not be correctly indicated when multiplying impacts at or near the computational limit of the model by the actual emissions. For long distances (greater than about 10 km) or tall stacks, all unit emission rates could be increased to 10, 100 or 1000 g/s for all sources.

- If sources are run in a single pass assuming no chemical transformation takes place (e.g., degradation or secondary formation), the air parameters from the air model will be slightly over-predicted or under-predicted, depending on the reactivity rate of the specific chemical and travel times in the atmosphere after release.

literature. As such, it may be most appropriate to communicate this information by developing a side-by-side comparison of the estimates of background concentration and risk to estimates of study area risk developed through the modeling exercise. An example approach for communicating information about background risk is provided in Section 6.2.2.

## 5.3 Estimating Inhalation Exposure

At the end of the dispersion modeling portion of the analysis, the risk assessment team will have estimates of chemical concentration at specified points throughout the study area. This section discusses how to take the results of the air dispersion modeling to the next step of the analysis - estimating exposure. The background for this discussion is found in ATRA Volume 1, Chapter 11, and analysts are encouraged to become familiar with that chapter before proceeding. Another key resource is EPA's *Guidelines for Exposure Assessment* (http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=15263).

**Information on Background Concentrations**

Several important information sources on general background concentrations are provided below. Additional information on background concentrations may be available in the scientific literature. Background information for a specific community can also be developed de novo, typically by monitoring.

**NATA National-Scale Risk Characterization**

The 1999 national-scale assessment provides background concentrations for 13 air toxics based on available monitored data. For the remainder of the air toxics in the assessment, EPA used values reported in technical literature as identified in the Cumulative Exposure Project (CEP; 15 air toxics), or the background concentration was assumed to be zero (105 air toxics) if no values were reported in the CEP. The values taken from the CEP were based on technical literature and are not representative of any particular year. For all 28 air toxics with estimated background concentrations, each census tract in a county is assigned the same county-specific background concentrations. The total estimated concentration for each pollutant in each census tract is the sum of the background and the modeled concentrations (from modeled emission sources). For a list of pollutants and background concentration distributions, see http://www.epa.gov/ttn/atw/nata1999/background.html.

**ATSDR Toxicological Profiles**

Estimates of ambient background concentrations for 275 substances are provided in the ATSDR Toxicological Profile series: http://www.atsdr.cdc.gov/toxpro2.html.

### 5.3.1 Inhalation Exposure Assessment DQOs

For the estimated ambient concentrations to be of use in evaluating exposures, they will have to meet certain minimum DQOs.[e] And like the other DQOs discussed in this chapter, a quick review will show the linkages back to the DQOs for emissions characterization and air dispersion modeling.

- **Time scale used to estimate exposure concentrations**. The ambient concentration estimates derived from air dispersion modeling must be pertinent to the time frames of the exposure periods of interest. Commonly, the air dispersion modeling should provide, at a minimum, an annual average concentration for an evaluation of chronic exposures.

  The model may also need to provide shorter term concentrations for an analysis of acute exposures. It is important that the planning and scoping phase of the assessment perform an analysis of the available acute toxicity data for the chemicals to be evaluated to identify the most pertinent averaging times to be produced by the dispersion modeling. Ideally, the averaging times of the acute toxicity values and those produced by the model should match. For example, an acute toxicity reference concentration with a one-hour averaging time should be compared to an estimate of ambient concentration that also has a one-hour averaging time.

- **Spatial scale**. The air dispersion modeling should provide estimates of ambient concentration at predetermined points throughout the modeling domain where the assessment of exposure is desired. This will commonly include all the points on the modeling grid, but may also include additional points such as census tract internal points, census block internal points, and special locations such as schools, hospitals, day care centers, and retirement centers.

- **Population activity data**. If an exposure model is subsequently applied to the air dispersion modeling results (see ATRA Volume 1, Chapter 11), it is important to assess whether the resolution of the emissions inventory, meteorological data, and activity patterns are temporally matched. For example, most emissions data are reported as a single aggregate amount released per year (e.g., tons per year). The exposure model, on the other hand provides activity patterns that may be reflective of hourly, daily, or seasonal time scales. emissions data, may result in misleading answers. Analysts need to carefully assess whether the application of an exposure model will provide any additional useful information (i.e., whether their DQOs for this exercise are achievable).

- **Analytical framework**. The DQOs developed for a study will depend on whether the analytical framework is deterministic (i.e., inputs and outputs are discrete, or "point" values) or stochastic (i.e., inputs and outputs are characterized by distributions representing variability and/or uncertainty). For example, when probability density functions (PDFs) are

[e] Model outputs are not truly "data" (although they are often referred to as such) because they are estimates of a value based on modeling rather than a measurement; therefore, it is not technically accurate to refer to data quality objectives for modeled exposure estimates. In this section, however, the phrase "DQO" is applied to exposure assessment for simplicity and consistency.

used to represent a particular activity pattern for individuals in a population, the DQO may stipulate the certainty associated with that PDF.

### 5.3.2 Developing the Exposure Concentration Estimates

The term *exposure concentration* (EC) is used to describe the concentration of a chemical in its transport or carrier medium (i.e., an environmental medium such as air or contaminated food) at the point of contact. This concentration can be either a monitored or modeled value and may or may not have been refined by the application of an exposure model. Some of the more common ways of developing an EC are provided in Exhibit 5-2 above. A background discussion on ECs is provided in ATRA Volume 1, Section 11.2.

Utilizing the unit emission rate approach discussed previously, the determination of the ambient concentration for each toxic air pollutant is typically a two-step process. First, the air dispersion modeling analysis computes the unit ambient concentration for each chemical for each point in the study area that was modeled. Each source (or group of sources) is modeled individually using this approach. This results in a unit ambient concentration from each source at each of the assessment point(s) of interest for each toxic air pollutant. For example, in a study area with 30 different sources, this step would require 30 separate air model runs.[f]

Second, the total ambient concentration for a specific toxic air pollutant at each assessment point may now be determined. For each source (or group of sources), the unit ambient concentration from the air modeling at each assessment point is multiplied by the emission rate of the specific toxic air pollutant. The resulting product is the ambient concentration for that specific toxic air pollutant at each assessment point from that source. The sum of the ambient concentrations for all sources of the specific toxic air pollutant at each assessment point is the predicted ambient concentration for that specific toxic air pollutant. This procedure is repeated for all air toxics of interest by multiplying the source-specific emission rate for each toxic air pollutant for each source by the unit ambient concentration from the air modeling for each source, and summing the products.

The resulting ambient air concentrations are then used to determine the EC in one of two ways (see Exhibit 5-8):[g]

- **Use the Unmodified Ambient Air Concentrations as a Surrogate for Exposure**. Concentrations of air toxics estimated by air dispersion models and/or measured at specific locations are often used as surrogates for the inhalation EC for the populations in the study locations. When used in a chronic lifetime exposure assessment, the underlying assumption, which should be made clear among the risk assessment team and explicitly stated in the risk characterization, is that the population of concern is breathing outdoor air continuously at the

[f] As noted previously, each combination of source and chemical emitted can be modeled without the use of unit emission rates. This approach allows for more refined modeling techniques (e.g., accounting for chemical-specific degradation characteristics) but also results in a greater number of model runs.

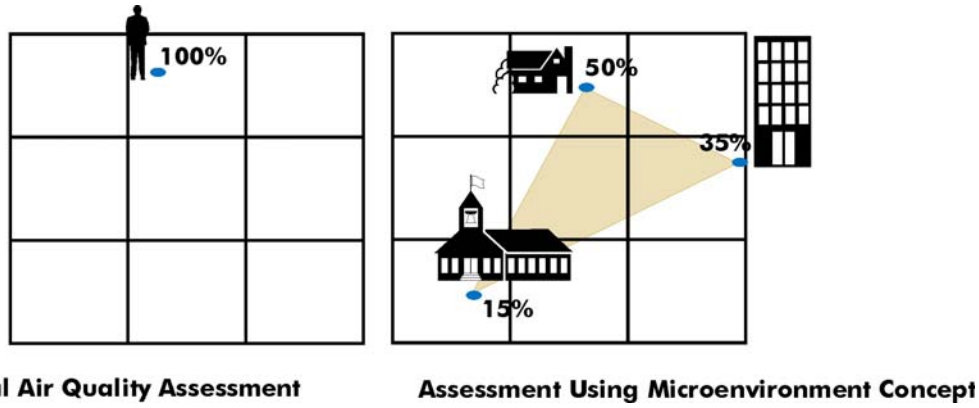
[g] This process can be done manually (with off-the shelf computer tools such as a spreadsheet) or it can be done automatically by some existing air toxics modeling tools (such as those in the RAIMI toolbox). When there are many sources and chemicals in an area, it is recommended that analysts consider using tools that have been specifically designed for this task.

specified location in question for a lifetime. As such, risk estimates developed using this approach are necessarily "screening-level" estimates of risk.

- **Refine the Ambient Air Concentration through Application of an Exposure Model** (e.g.,TRIMExpo, HAPEM5; see http://www.epa.gov/ttn/fera/). Concentrations of air toxics estimated by air dispersion models at specific locations are combined with demographic information about people in the study area, their activity patterns, and microenvironment concentrations. The assessment objective is to develop a refined estimate of EC by taking into account the different concentrations in the different locations (or microenvironments) in which people in the study area interact with the contaminated air being evaluated (see Exhibit 5-8). A more complete discussion of exposure modeling is provided in ATRA Volume 1, Chapter 11.

A **microenvironment** is a small 3-dimensional space (e.g., an office, a room in a home, a garden, a car) in which people spend their time during their daily routine that is treated as homogeneous (or well characterized) with regard to the exposure concentration for one or more air pollutants.

**Exhibit 5-8. Two General Ways to Estimate Inhalation Exposure Concentration**




The left-hand side illustrates the use of ambient air concentrations as a surrogate for the EC. In this example, the analysis assumes that individuals spend 100 percent of their time at a given location, so the estimate of ambient concentration = EC. The right-hand side illustrates the use of exposure modeling. In this example, the analysis assumes that an individual spends 50 percent of his/her time at home; 15 percent at a school; and 35 percent at an office. The exposure model also takes into consideration that the indoor air concentrations at each location (indoor microenvironment) are different than the corresponding outdoor ambient air concentrations. The EC is the weighted sum of the product of the ambient concentrations at each location and the amount of time spent there. Both outdoor and indoor concentrations of air are usually considered at each location (see ATRA Volume 1, Chapter 11).

### 5.3.3 Representing Exposures in the Study Area

At the end of the air dispersion modeling study (and possibly after the further application of an exposure model), the analysts will be in a position to describe exposures across the study area. There are many ways to do this, such as evaluating exposure at specific locations (e.g., the areas with the highest or lowest predicted ECs). Descriptions of exposures may be limited to all residentially zoned areas or may focus specifically on locations where people are known to currently reside. In contrast, some assessments may decide to also display exposures at businesses in the area or at more generalized points (e.g., a census tract centroid). Other options for displaying exposure include isopleths of EC and population exposures (i.e., the numbers of people at a given exposure level). The ways to represent exposure are analogous to risk representations. An introduction to this topic is provided in ATRA Volume 1, Chapter 13 and illustrated further in the next chapter.

## 5.4 Toxicity Assessment

The purpose of the toxicity assessment is to weigh available evidence regarding the potential for toxicity in exposed individuals (**hazard identification**) and to quantify the toxicity by deriving an appropriate dose-response value (**dose-response assessment**). Much of the work of identifying the potential health effects of common urban pollutants and developing toxicity factors for them has already been accomplished. EPA has identified the resulting peer-reviewed toxicity information and dose-response values for these chemicals at http://www.epa.gov/ttn/atw/toxsource/summary.html. Where multiple sources of this information are available for a particular chemical, a hierarchy has been applied for the purposes of screening level assessments. (Note that these and other toxicity values are subject to change as new information and analyses become available, and the analyst is encouraged to check for the most recent data when carrying out an assessment.) For more complex, refined risk assessments (i.e., those developed to support regulatory decisions for particular sources or substances), analysts may evaluate dose-response in detail for each "risk driver" to incorporate appropriate new toxicological data.

In most air toxics risk assessments, the development or evaluation of new toxicological data will not generally be required. However, it is important for analysts to understand how the available toxicity data were developed in order to both select and use toxicity values appropriately and to be able to describe their associated uncertainties (see ATRA Volume 1, Chapter 13). A basic understanding of toxicity assessment will also aid in identifying and filling significant data gaps, interpreting the results of the risk analysis, and communicating the results to stakeholders. To that end, ATRA Volume 1, Chapter 12, is repeated here to provide an overview of this topic. (Stakeholders are cautioned that the evaluation and interpretation of toxicity data for risk assessment purposes generally requires specialized toxicological expertise; as such, a toxicologist with the appropriate background should be part of the partnership team.)

### 5.4.1 Hazard Identification and Dose-Response Information

As part of the hazard identification step, evidence is gathered from a variety of sources regarding the potential for an toxic air pollutant to cause adverse health effects in humans. These sources may include human data, experimental animal studies, and supporting information such as *in*

*vitro* laboratory tests. The source of data affects the overall uncertainties in the resulting human dose-response values, as discussed below.

- **Human data**. Human toxicity data associated with exposures to air toxics may be located in epidemiological studies, controlled exposure studies, or studies of accidental exposures. Well-conducted epidemiological studies that show a positive association between exposure to a chemical and adverse health effects often provide evidence about human health effects associated with chronic exposures. Such data, however, are available only for a limited number of air toxics. Epidemiological data also are very difficult to interpret, because the number of exposed individuals may be small, the incidence of effects may be low, doses are usually not well-characterized, and there may be complicating factors such as simultaneous exposure to multiple chemicals and heterogeneity among the exposed group in terms of age, sex, diet, and other factors. Controlled exposure studies provide stronger evidence, since both the exposure duration and exposure concentrations are more accurately known. However, such studies with humans are generally limited to acute exposure durations. Studies reporting health effects associated with accidental exposures may be helpful, although exposure concentrations to air toxics may be high, and effects may be acute rather than chronic. Also note that small sample size is often a significant limitation to interpreting controlled and accidental exposure studies.

> **Epidemiology** is the study of the distribution and determinants of disease or health status in a population.

- **Animal data**. The toxicity database for most air toxics is drawn from experiments conducted on non-human mammals such as rats, mice, rabbits, guinea pigs, hamsters, dogs, or monkeys. The underlying assumption is that the susceptibility of humans and these animals to the effects of the chemicals is broadly similar because we share many common biological attributes (e.g., similar organs, similar and, in some cases, identical metabolic processes). However, some observations in animals may be of uncertain relevance to humans (e.g., if tumors are observed in an animal experiment, but the organ in which the tumor is formed does not exist in humans). Also, it is necessary to adjust the results from animal studies to humans due to differences in body mass, anatomy, metabolic rate, and other species-specific factors (see, for example, ATRA Volume 1, Section 5.6.3). This is why derivation of dose-response values from animal studies requires considerable expertise.

- **Supporting data**. Metabolic, pharmacokinetic, and genotoxicity studies are sometimes used to infer the likelihood of adverse effects in humans. Metabolic studies on absorption, distribution, metabolism, and elimination can provide information about the mechanisms of toxicity associated with a particular chemical in humans. In physiologically based pharmacokinetic (PBPK) models,[h] the body is subdivided into a series of anatomical or physiological "compartments" that represent specific organs or lumped tissue and organ groups, and the behavior of the chemical is modeled in each compartment. Data on a chemical's pharmacokinetics, genotoxicity, and possible mode of action can be used to refine a toxicity assessment. In some cases, computer models using structure-activity relationships (i.e., predictions of toxicological activity based on analysis of chemical structure) also may

[h] A PBPK model estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion.

be used as supporting evidence. EPA considers these types of data to be supportive, not definitive, evidence of a chemical's toxicity.

Information from these sources is considered in the hazard and dose-response assessment steps in characterizing a chemical with regard to the type(s) of effect a chemical produces (the hazard) and the circumstances in which this occurs, as well as the level of exposure required to produce that effect. The output of the dose-response assessment is the relationship between **dose** (the level of exposure) and the resulting **response** (the increased incidence and/or severity of adverse effects). A dose-response assessment is the process of quantitatively evaluating toxicity information, characterizing the relationship between the dose of the contaminant received (or the inhalation exposure concentration, for inhalation assessments) and the incidence of adverse health effects in the exposed subjects (which may be animal or human) and then, as appropriate, extrapolating these results to human populations. Depending on the type of effect and the chemical, there are two types of dose-response values that traditionally may be derived: predictive cancer risk estimates, such as the **inhalation unit risk estimate (IUR)**, and predictive non-cancer estimates, such as the **reference concentration (RfC)**.[i] Both types of dose-response values may be developed for the same chemical, as appropriate.

**Inhalation Dose-Response Values**[a]

**Inhalation Unit Risk (IUR)**: The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent via inhalation per $\mu g/m^3$ over a lifetime. The interpretation of the IUR would be as follows: if IUR = $2 \times 10^{-6}$ $\mu g/m^3$, not more than 2 excess tumors are expected to develop per 1,000,000 people if exposed continuously for a lifetime to 1 µg of the chemical per cubic meter of inhaled air. The number of expected tumors is likely to be less; it may even be none.

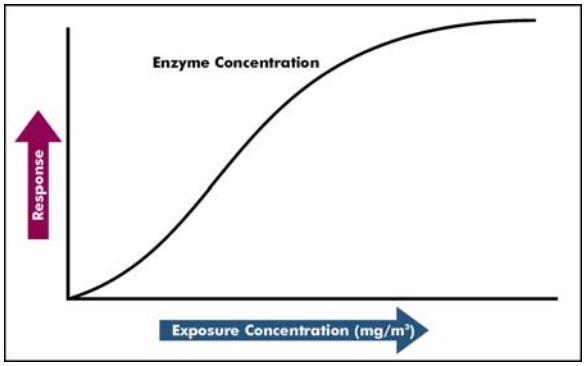
**Reference Concentration (RfC)**: An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive sub-populations) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Generally used in EPA's noncancer health assessments.

[a]The phrase "dose-response" is used generally here and elsewhere in the document. EPA's values for inhalation, however, are derived for exposure concentration, although with consideration of dose. Consideration of the relationship between exposure concentration, dose, and dosimetry (how the body handles a chemical once it is inhaled) is inherent in the derivation of these exposure concentration-response values.

The relationship of dose to response can be illustrated as a graph called a **dose-response curve**. There are two general types of response data that may be considered and graphed. One is termed "continuous" and refers to responses such as the severity in changes to a physiological parameter in a given individual as dose increases (see Exhibit 5-9, A) . The second describes the incidence of a particular response in a population (see Exhibit 5-9, B). By convention, dose or exposure is represented on the x-axis; response on the y-axis (Exhibit 5-9).

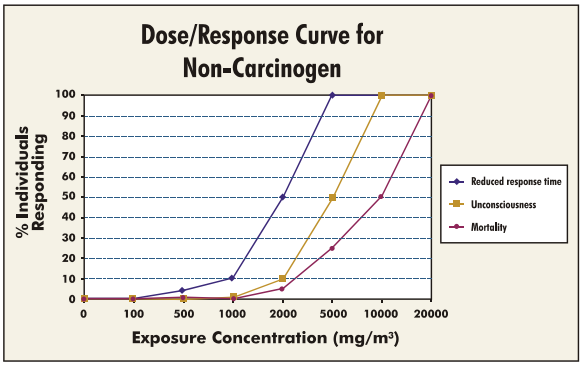
[i] While the majority of RfCs are derived for effects other than cancer, RfCs may be derived for all effects, including cancer, when a non-linear mode of action has been demonstrated for carcinogenicity.

**Exhibit 5-9. Examples of Dose-Response Curves**




**A. Continuous Response Data**

Simple example of a dose-response curve for graded responses of a specific physiological parameter to increasing exposure.




**B. Different Responses in a Population**

Simple example of the incidence of three different effects in an exposed population in response to different exposure concentrations (over the same duration).

While the primary focus of this chapter is on description of dose-response values relevant to chronic (long-term) exposures, the information reviewed for developing those values may include effects associated with acute (short-term) exposures. Additionally, information on acute exposures is essential to the development of acute exposure reference values (see Section 5.9).

- **Acute exposures** are usually relatively short in duration, but relatively high in concentration and may result in immediate respiratory and sensory irritation, chemical burns, narcosis, eye damage, and various other effects. Acute exposures also may result in longer-term health effects.

- **Chronic exposures** are usually relatively long in duration, but relatively low in concentration and may result in health effects that do not show up immediately and that persist over the long term, such as cardiovascular disease, respiratory disease, liver and kidney disease, reproductive effects, neurological damage, and cancer.

Generally, chronic reference values are derived for exposure periods between seven years and a lifetime. Acute reference values (see Section 5.9) are generally developed for very short exposures (e.g., hours to days; Exhibit 5-10). For intermediate exposures, subchronic reference values are available from some sources (e.g., ATSDR). Most air toxics risk assessments will focus on chronic and acute evaluations; however, under more limited circumstances, subchronic evaluations may be performed.

| Exhibit 5-10. Reference Values of Different Durations |
|---|
| In the Agency's *Review of the Reference Dose and Reference Concentration Processes*,[3] it was recommended that in addition to the traditional chronic reference value (i.e., RfC or RfD) included in the IRIS database, values of several shorter durations also be developed, where possible. As a first step in this direction, the *Review* proposed the following definitions. EPA currently is considering these and other recommendations made in the *Review*. These definitions are based on exposure durations for humans, and were not intended to be rigid specifications, but simply general descriptions of the relevant exposure time period.<br><br>• **Acute**: Exposure by the oral, dermal, or inhalation route for 24 hours or less.<br><br>• **Short-term**: Repeated exposure[a] by the oral, dermal, or inhalation route for more than 24 hours, up to 30 days.<br><br>• **Longer-term**: Repeated exposure by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the life span in humans[b] (more than 30 days up to 90 days in typically used laboratory animal species[c]).<br><br>• **Chronic**: Repeated exposure by the oral, dermal, or inhalation route for more than approximately 10 percent of the life span in humans (more than approximately 90 days to 2 years in typically used laboratory animal species). |
| [a]A repeated exposure may be either continuous, periodic, or intermittent. A continuous exposure is a daily exposure for the total duration of interest. A periodic exposure is one occurring at regular intervals (e.g., inhalation exposure 6 hours/day, 5 days/week; or oral exposure 5 days/week). An intermittent exposure is one in which there is no effect of one exposure on the effect of the next; this definition implies sufficient time for the chemical and its metabolites to clear the biological system before the subsequent (i.e., noncumulative pharmacokinetics). A periodic exposure may or may not be intermittent.<br><br>[b]An average of 70 years is typical default used for chronic exposures.<br><br>[c]Examples of typically used laboratory species include rats, mice, and rabbits. |

### 5.4.2 Dose-Response Assessment Methods

Depending on whether a substance causes cancer and whether its dose-response curve is thought to have a threshold, EPA may use either of two approaches in a dose-response assessment. One approach produces a predictive estimate (e.g., inhalation cancer risk estimate), and the other produces a reference value (e.g., RfC). Historically, the use of a predictive estimate has been limited to cancer assessment. That is, dose-response assessments for cancer have been expressed as predictive cancer risk estimates based on an assumption that any amount of exposure poses some risk. Assessments of effects other than cancer usually have been expressed as reference values at or below which no harm is expected. Many substances have been assessed both ways: the first for cancer and the second for adverse effects other than cancer. While this use of predictive estimates for cancer and reference values for other effects is still the practice for the vast majority of chemicals, EPA now recognizes that there are chemicals for which the data support an alternate approach.

An important aspect of dose-response relationships is whether the available evidence suggests the existence of a threshold. For many types of toxic responses, there is a **threshold dose** or

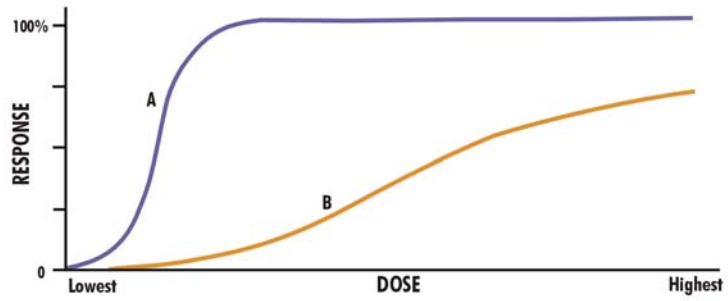
dose rate below which there are thought to be no adverse effects from exposure to the chemical. The human body has defenses against many toxic agents. Cells in human organs, especially in the liver and kidneys, break down many chemicals into less toxic substances that can be eliminated from the body in urine and feces. In this way, the human body can withstand some chemical exposure (at doses below the threshold) and still remain healthy. For example, many air toxics are naturally occurring substances to which people routinely receive trace exposures at non-toxic levels.

Identification of a threshold dose depends on the type of response and the way in which the toxic chemical produces it. EPA has developed guidelines[4] for assessing the dose-response for various types of adverse effects, which provide more information about evaluating evidence to determine if a threshold exists.

> *All substances are poisons: there is none which is not a poison. The right dose differentiates a poison and a remedy.*
> – Paracelsus

Both the point at which the dose-response curve begins to ascend (its threshold, which may be zero) and the slope of the curve (its steepness) provide information about the toxicity of a chemical (Exhibit 5-11). The potency of a chemical is a measure of its strength as a toxicant compared with other chemicals. Therefore, the lower the threshold dose, the more potent (or toxic) the chemical. The slope of the curve is a measure of the range of doses from the threshold dose (at which the adverse effect is first measured) to the dose at which the effect is complete (i.e., higher doses produce no additional incidence of that effect, although other adverse effects may begin to appear). The steeper the dose-response curve, the smaller the range between the first appearance of an effect and a substantial response.

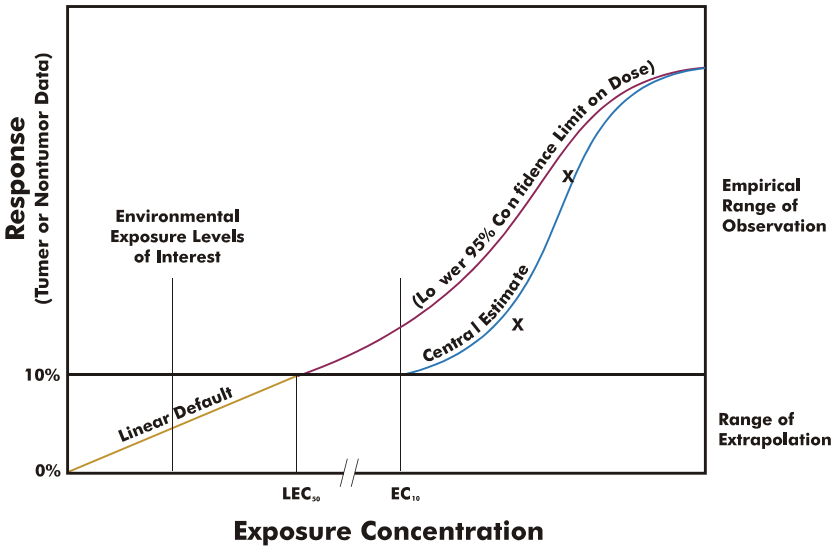
**Different Responses Exhibit Different Dose-Response Curves**




Line A – A sharp increase in response with increasing dose
Line B – A more gradual increase in response with increasing dose

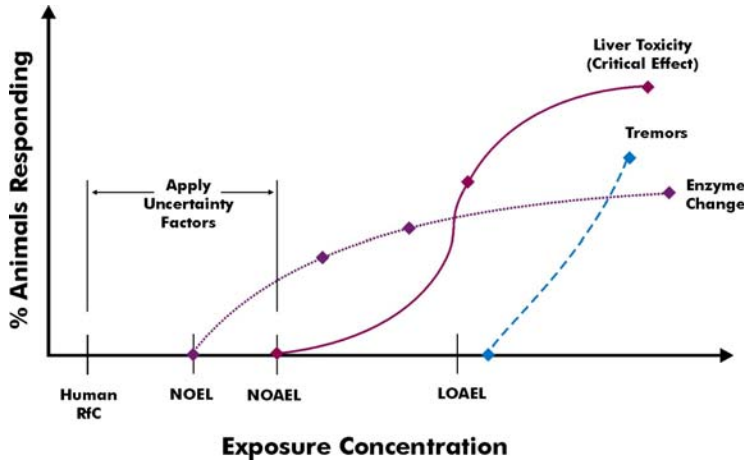
**Exhibit 5-11. Dose-Response Relationships for Carcinogens and Noncarcinogens**

**A. Example Linear Carcinogen**




In the absence of clear evidence to the contrary, EPA assumes as a matter of science policy that even a very low exposure to a cancer-causing pollutant can increase the risk of cancer (albeit a small amount). Experimental data are used to construct a dose-response relationship and identify the point of departure – the dose that can be considered to be near or in the range of observed responses and, thus, no significant extrapolation is needed. To estimate the dose-response relationship at doses below the point of departure, the dose-response relationship between the point of departure and zero is assumed to be linear. Thus, at doses below the point of departure, with each unit of increase in exposure (dose), there is an increase in cancer response. Where evidence supports the acceptance of a non-linear mode of action, a reference concentration approach may be employed, as shown in "B" below. $LEC_{50}$= lethal effective concentration for 50 percent of the population; $EC_{10}$= effective concentration that causes an observable adverse effect in 10 percent of the population.

**B. Example Non-linear Approach**




A dose may exist below the minimum health effect level for which no adverse effects occur. EPA typically assumes that at low doses the body's natural protective mechanisms prevent or repair any damage caused by the pollutant, so there is no ill effect at low doses. Even long-term (chronic) exposures below the threshold are not expected to have adverse effects. The dose-response relationship (the response occurring with increasing dose) varies with pollutant, individual sensitivity, and type of health effect. NOEL = no-observed-effect-level; NOAEL = no-observed-adverse-effect-level; LOAEL = lowest-observed-adverse-effect-level.

Epidemiologic and toxicologic data on air toxics typically result from exposure levels that are high relative to environmental levels. Therefore, **low-dose extrapolation** (prediction) is necessary to derive an appropriate dose-response value. For a few air toxics (e.g., the criteria air pollutants ozone and carbon monoxide), data are sufficient to characterize dose-response relationships at environmental levels. In such cases, there is no need for extrapolation of toxicity data to lower doses. Such is not the case for most air toxics. Low-dose extrapolation requires either information or assumptions about the type of dose-response curve likely under low dose situations. EPA risk assessment guidelines provide more detailed information on how EPA performs low-dose extrapolation for chemicals with various toxic effects, such as developmental effects or neurotoxic effects.[4]

### 5.4.3 Hazard Identification

The hazard identification, which is usually part of an existing dose-response assessment for each chemical, provides a summary of the available toxicity information for the air toxics being studied, and includes the weight of evidence determination and identification of critical effects. This step should answer the following questions:

**Items to Include in the Hazard Identification of an Air Toxics Risk Assessment**

- List of chemicals detected
- Summaries of toxic effects and quality of the toxicological evidence
- Discussion that focuses the risk assessment on chemicals most likely to cause adverse effects

- Can exposure to a chemical be linked causally to particular health effects?
- Could these effects occur at environmentally relevant concentrations?
- What is the nature and strength of the evidence of causation?

By definition, all HAPs and many other air toxics have the potential to cause adverse effects in the exposed population. Exhibit 5-12 provides examples of cancer and non-cancer effects. Appendix C of ATRA Volume 1 identifies which HAPs have been associated with carcinogenic (cancer) effects or non-cancer effects, along with the strength and ratings of the toxicity evidence that has been evaluated by EPA or other international environmental agencies.

| Exhibit 5-12. Examples of Adverse Health Effects |
|---|
| • Birth defects<br>• Tremors<br>• Infertility<br>• Skin rash<br>• Melanoma |

An air toxics risk assessment should include in its hazard identification a summary of the quality of the toxicological evidence (i.e., the nature and strength of the evidence of causation) for the chemicals of concern. Study factors such as the route of exposure used, the type and quality of health effects, the biological plausibility of findings, and the consistency of findings across studies all contribute to the strength of the hazard identification statement.

#### 5.4.3.1 Weight of Evidence – Human Carcinogenicity

A major determination made during the hazard identification step concerns the potential of a chemical to cause cancer in humans. This determination, which involves considering (or weighing) all the available evidence, is called the weight of evidence determination. This determination is complicated by possible inadequacies of the published studies, as well as differences in body processes between people and laboratory animals. EPA's *Guidelines for Carcinogen Risk Assessment* guide scientists in interpreting available studies to assess the potential human carcinogenicity of environmental pollutants. (EPA's carcinogen risk assessment guidelines were first published in 1986. Revisions were proposed in 1996 and 2001 and the July 1999 draft of the revisions was adopted as interim guidance. A subsequent 2003 draft of the Guidelines has been released for public and scientific review prior to adoption as final. The guidelines are available on the web.)[5] When compared with EPA's original 1986 guidelines, the 1999 interim Guidelines recommend a more comprehensive evaluation of the evidence with regard to a chemical's potential mode of action, and a more complete description of the context of a chemical's carcinogenic potential (e.g., "likely carcinogenic by inhalation and not likely carcinogenic by oral exposure"). The weight of evidence determination now includes one of five descriptors, and is accompanied by additional text that more completely summarizes EPA's interpretation of the evidence. The narrative statements consider the quality and adequacy of data and the consistency of responses induced by the agent in question (see Exhibit 5-13).

| **Exhibit 5-13. Information Regularly Included in a Narrative Statement Describing the Characterization of Weight of Evidence for Carcinogenicity (1999 Interim Guidelines)** |
|---|
| • Name of agent and Chemical Abstracts Services number, if available<br>• Conclusions (by route of exposure) about human carcinogenicity, using one of five standard descriptors: "Carcinogenic to Humans" "Likely to be Carcinogenic to Humans" "Suggestive Evidence of Carcinogenicity, but Not Sufficient to Assess Human Carcinogenic Potential" "Data are Inadequate for An Assessment of Human Carcinogenic Potential" "Non Likely to be Carcinogenic to Humans".<br>• Summary of human and animal tumor data on the agent or its structural analogues, their relevance, and biological plausibility<br>• Other key data (e.g., structure-activity data, toxicokinetics and metabolism, short-term studies, other relevant toxicity or clinical data)<br>• Discussion of possible mode(s) of action and appropriate dose-response approach(es)<br>• Conditions of expression of carcinogenicity, including route, duration, and magnitude of exposure<br><br>*Source*: EPA (1999) *Guidelines for Carcinogen Risk Assessment. Review Draft*[5] |

The *2005 Guidelines* place particular importance on the consideration of a chemical's mode of action (MOA) and emphasize an analysis of the available data with regard to the key events inherent in how exposure to a chemical results in cancer. In addition to being critical to selection of the dose-response approach (see Section 5.6.3), performance of such an analysis as part of the cancer hazard characterization is critical to the *2005 Supplemental Guidance,* which provides specific guidance on potency adjustment for carcinogens acting through a mutagenic

MOA.[j] [See Farland 2005 memo at http://www.epa.gov/osa/spc/pdfs/canguid1.pdf for information on applying the *Guidelines* MOA framework in determining whether a chemical has a mutagenic MOA).] For example, when assessing cancer risk for exposures early in life for such chemicals, the *Supplemental Guidance* recommends use of default adjustment factors if no chemical-specific data on early life exposure-response were available for use in the development of the dose-response assessment (see Chapter 6 of the *Supplemental Guidance* for more information).[k] Where such data are available, the *Supplemental Guidance* recommends that they be used (regardless of the chemical's MOA) in developing the dose response assessment for that chemical, with attention to any lifestage-specific differences in potency.[l] Information on how the Agency is implementing the *2005 Cancer Guidelines* and *Supplemental Guidance* is available on the Agency's web site (see www.epa.gov/cancerguidelines and http://www.epa.gov/osa/spc/cancer.htm).

Many existing carcinogen assessments were developed pursuant to EPA's 1986 *Guidelines for Carcinogen Risk Assessment*, which used a simpler but less informative weight of evidence system (see Exhibit 5-14).

Information bearing on the qualitative assessment of carcinogenic potential may be gained from human epidemiological data, animal studies, comparative pharmacokinetic and metabolism studies, genetic toxicity studies, structure-activity relationship (SAR) analysis, and other studies of an agent's properties. Information from these studies helps to elucidate potential modes of action and biological fate and disposition.

Upon such consideration, both EPA systems assign a consensus interpretation to the weight of evidence, evaluating the likelihood that the agent is a human carcinogen. Toxicological evidence is characterized separately for human studies and animal studies as: sufficient, limited, inadequate, no data, or evidence of no effect. The characterizations of these two types of data are combined, and based on the extent to which the agent has been shown to be a carcinogen in experimental animals or humans, or both, the chemical is given a weight of evidence classification.

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[j] As explained in the *2005 Guidelines* (p. 1-10), a carcinogenic "mode of action" is a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in the formation of cancer. Simply stated, the MOA explains processes that may result in disease following chemical interruption of normal cellular activity. Cancer refers to a group of diseases involving abnormal, malignant tissue growth. The development of cancer involves a complex series of steps, and carcinogens may operate in a number of different ways. Ultimately, cancer results from a series of defects in genes controlling cell growth, division, and differentiation. Thus, all cancers caused by chemicals will have mutations. At issue is how the mutations originated, i.e., the MOA. The Agency intends to issue a document describing considerations in assessing the potential for a chemical to have a mutagenic MOA.

[k] For example, when the IRIS assessment for a chemical states that a weight of evidence evaluation supports a determination that a chemical is carcinogenic by a mutagenic mode of action, and chemical specific potency estimates reflecting lifestage susceptibility have not been derived, the risk assessor would utilize that determination and the appropriate application of recommended age dependent adjustment factors with age-specific estimates of exposure and the chemical's IRIS inhalation cancer slope factor (see Chapter 6 of the *Supplemental Guidance*).

[l] In the absence of chemical-specific data indicating differential early-life susceptibility or when the MOA is not mutagenicity, it is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) in the dose-response assessment provides adequate public health conservatism.

| Exhibit 5-14. EPA's Weight of Evidence Classification for Carcinogens (1986 Guidelines) | |
|---|---|
| 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 with 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) |
| *Source*: EPA (1986). *Guidelines for Carcinogen Risk Assessment*[5] | |

Generally, no single factor is determinative. For example, strength of association is one of the criteria for causality. A strong association between exposure and cancer in animals is more likely to indicate causality than a weak association. However, finding of a large cancer incidence in a single study must be balanced against the lack of consistency as reflected by null results from other equally well-designed and well-conducted studies. In this situation, the positive association of a single study may either suggest the presence of chance, bias, confounding factors, or different exposure conditions. On the other hand, evidence of weak but consistent associations across several studies suggests either causality or that the same confounder may be operating in all of these studies.

If information is available to consider the mode of action for carcinogenicity, the carcinogenicity assessment will evaluate that information and draw conclusions that influence the dose-response method for the substance. If the evidence is sufficient to support a conclusion of nonlinear dose-response, then the information on carcinogenicity may be considered in combination with the information on other effects in deriving a reference value such as an RfC (see Section 5.7). Otherwise, a linear dose-response approach leading to a predictive risk estimate, such as an IUR, will usually be pursued. If the information supports it, the guidelines also accommodate the development of a non-linear predictive risk estimate.

**Biological Effects of Carcinogens**

**Carcinogens** are chemicals that induce cancers. Examples include:

- *4-Aminobyphenol*, which targets the bladder;
- *Benzene*, which targets the tissue that make white blood cells;
- *Asbestos*, which targets the lung's tissue;
- *Benzidene*, which targets the bladder;
- *Beryllium*, which targets the lungs;
- *Chromium*, which targets the respiratory tract;
- *Radionucleotides*, which targets bone marrow and the lungs; and
- *Vinyl chloride*, which targets the liver.

There are various types of carcinogens, including:

- **Primary Carcinogens**: A primary carcinogen is a substance that is carcinogenic as it occurs in the environment.
- **Procarcinogen**: A procarcinogen is a substance that becomes carcinogenic only after conversion from some benign form. Most environmental carcinogens are of this type.
- **Cocarcinogen**: A cocarcinogen is a substance that is not carcinogenic by itself, but potentiates the carcinogenic effect of other chemicals.

Chemicals also can serve as **mutagens**, causing changes in genetic material that can disrupt cell function and lead to cancer or other health problems.

### 5.4.3.2 Identification of Critical Effect(s) – Non-Cancer Endpoints

As part of the characterization of the available information on non-cancer health effects (or including cancer, if a threshold mode of action has been established), the targets of chemical toxicity within the body are identified, along with what have been termed "critical effects" associated with the toxicity. A **critical effect** is described as "either the adverse effect that first appears in the dose scale as dose is increased, or as a known precursor to the first adverse effect." Underlying this designation is the assumption that if the critical effects are prevented, then all other adverse effects observed at higher exposure concentrations or doses are also prevented.[m] Note that not all observed effects in toxicity studies are considered adverse effects. The identification of the critical effect(s) depends on a comprehensive review of the available data with careful consideration of the exposure conditions associated with each observed effect, so that comparisons of effect levels or potential reference values are made on a common basis (see Section 5.7). A more comprehensive discussion of hazard identification and the evaluation of the underlying database for non-cancer effects is included in the EPA documents *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (1994) and *A Review of the Reference Dose and Reference Concentration Process* (2002).[6]

[m] A similar, more recent term, "key event," is defined as "an empirically observed precursor" to an adverse effect (e.g., liver cancer or other liver toxicity) consistent with a particular mode of action. The phrase "mode of action" refers to the way a given chemical may act in the body to initiate one or more adverse effects.

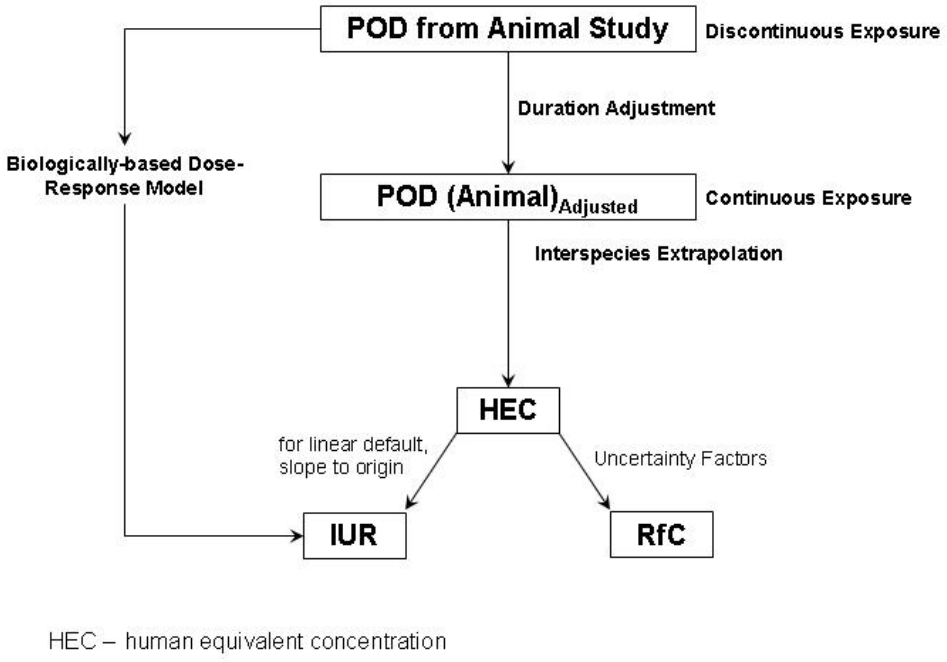
### 5.4.4 Dose-Response Assessment for Cancer Effects

The process for deriving a quantitative dose-response estimate for cancer (e.g., a cancer slope factor) involves the following three steps:

1. Determination of the concentration associated with the point of departure or POD (Section 5.6.1);
2. Derivation of the human equivalent concentration corresponding to the POD (Section 5.6.2); and
3. Extrapolation from the POD (expressed as human equivalent concentration) to derive carcinogenic potency estimates (Section 5.6.3).

The first two steps are also performed in the derivation of reference values such as the RfC (Exhibit 5-15); in that case, these steps are followed by the application of uncertainty factors (see Section 5.7).

**Exhibit 5-15. Steps involved in deriving an RfC or IUR From an Animal Study**



#### 5.4.4.1 Determination of the Point of Departure (POD)

Dose-response assessment for cancer and other effects begins with identification of the point of departure (an exposure concentration or intake) from the experimental data. This point (in terms of its human equivalent), while within the range of observation, is the point from which extrapolation begins, either for the purposes of deriving a cancer risk estimate (the IUR) or a RfC for non-cancer health effects.

**Example POD for Benzene**

EPA's characterization of the carcinogenic effects of benzene was updated in 1998. The IUR for benzene is based on epidemiologic studies showing clear evidence of a causal association between exposure to benzene and leukemia. The specific mechanisms by which benzene and its metabolites lead to cancer remain uncertain.

EPA selected the Rinsky et al. 1981 epidemiologic study of 1,165 Pliofilm rubber male workers at three facilities in Ohio as the data set for the dose-response relationship for determining the IUR. The workers had been employed between 1940 and 1965 and were followed through 1981. Rinsky et. al. expanded the study to include additional workers and published it in 1987. The Rinsky data suffers - as many epidemiologic studies do - from uncertainties about exposure levels in the early years. There are no measurements of benzene in the facilities' air prior to 1946, so exposures for these years must be estimated.

Using one set of exposure estimates with the Rinsky et al. study, EPA concluded that exposure to benzene increases the risk of leukemia at a level of 40 ppm-years of occupational exposure (8 hours/day, 5 days/week, 50 weeks/year). Below this number, the shape of the dose-response curve cannot be determined. Converting the occupational exposure of 40 ppm-years to an equivalent lifetime of environmental exposure yields 120 ppb, as a POD, below which the shape of the dose-response curve is uncertain.

EPA decided there is not sufficient evidence to demonstrate that the dose-response relationship below the POD is non-linear. As a science policy default, EPA assumed low-dose linearity for extrapolation from the POD to zero. Given a range of plausible exposure estimates for the Rinsky et al. study, the Agency determined that the benzene inhalation unit risk at 1 $\mu g/m^3$ ranges from $7.1 \times 10^{-3}$ to $2.5 \times 10^{-2}$ depending on the exposure estimates and modeling approach used to derive the POD.

*Source*: U.S. EPA. 1998. *Carcinogenic Effects of Benzene: An Update*. Office of Research and Development, National Center for Environmental Assessment, Washington, D.C. EPA/600/P-97/001F.; Rinsky, R.A., Young, R.J., and Smith, A.B. 1981. Leukemia in benzene workers. *American Journal of Industrial Medicine*. 2(3) 217:245.

The POD may be the traditional no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL), or **benchmark concentration (BMC)**.[(n)] EPA has recommended the use of the BMC approach, where possible, because the traditional use of the LOAEL or NOAEL in determining the POD has long been recognized as having several limitations (and generally is not used in dose-response for cancer effects. In particular, the LOAEL-NOAEL approach:

[n] Note that the corresponding value for ingestion exposures is the benchmark dose (BMD). This often is used as the general term for the BMC/BMD process.

- Is limited to one of the doses in the study and thus is dependent on study design;
- Does not account for variability and uncertainty in the estimate of the dose-response relationship;
- Does not account for the slope of the dose-response curve; and
- Cannot be applied, where there is no NOAEL, except through the application of an uncertainty factor.

If the dose-response data are of high quality, a mathematical dose-response model may be fitted to the data to determine a more precise POD than the NOAEL or LOAEL. When a model is used, the POD is calculated as the statistical lower confidence limit of the dose at which there is a low toxic response (usually 5 or 10 percent incidence in populations with an effect or a change in a physiological measurement indicating adversity).[7] The selection of the response percentage is intended to coincide with the sensitivity limit of the experimental design or professional judgment. This calculated POD is called the BMC.

The BMC approach is an alternate way of determining the point of departure for low-dose extrapolation. It can be used in cancer and noncancer risk assessment as the starting point for linear low-dose extrapolation, calculation of a margin of exposure, or application of uncertainty factors for calculating RfCs or other dose-response values. BMC methods involve fitting various mathematical models for dose-response to reported data and using the different results to select a BMC that is associated with a predetermined benchmark response, such as a 10 percent increase in the incidence of a particular lesion or a 10 percent decrease in body weight gain (Exhibit 5-16). EPA has developed the Benchmark Dose Software (BMDS) to facilitate these operations. BMDS currently offers 16 different mathematical models that can be fit to the laboratory data. EPA plans to continually improve and expand the BMDS system.[7]

It is likely that there will continue to be situations that are not amenable to BMC modeling and for which a NOAEL or LOAEL approach should be used. In some cases, there may be a combination of benchmark doses and NOAELs to be considered in the assessment of a particular agent.

#### 5.4.4.2 Derivation of the Human Equivalent Concentration

Because inhalation toxicity studies typically involve discontinuous exposures (e.g., animal studies routinely involve inhalation exposures of 6 hours per day, 5 days per week), the POD will usually need to be extrapolated to a continuous exposure scenario (as appropriate for the RfC and IUR). This duration adjustment step is essential in interpreting inhalation studies, but is not routinely necessary for the interpretation of oral exposures. Operationally, this is accomplished by applying a concentration-duration product, or **C × t product**[o] for both the

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[o] "C × t" is a component of Haber's Law that refers to the default assumption (in lieu of information to the contrary) that effects observed are related to the cumulative exposure or "area under the curve" (quantified by concentration, C, multiplied by duration, t). It is noted that when going from a discontinuous inhalation exposure regiment to a continuous exposure, the result will always be a lower value for concentration, thus providing an automatic margin of protectiveness for chemicals for which C alone (vs. C × t) may be appropriate, while providing the appropriate conversion for substances for which cumulative exposure is the appropriate measure.[4]

**Exhibit 5-16. Example Derivation of Benchmark Dose Level**

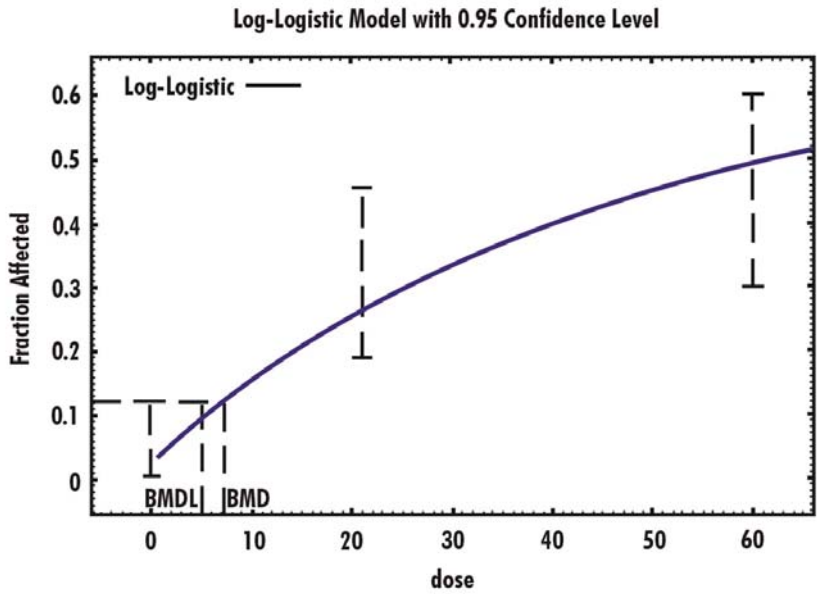



Illustration of the computation of a benchmark dose (BMD) and BMDL (a lower one-sided confidence limit on the BMD) for an extra risk of 0.10 (as suggested by the BMDS guidance document), using a one-sided 95 percent confidence interval. A number of models were fit to the data, and the log-logistic model illustrated provides the best fit to the example data. The predicted curve comes well within the confidence limits for each data point. Other data and models are illustrated in examples provided in the BMDS guidance document.[7]

number of hours in a daily exposure period and the number of days per week that the exposures are performed. For example, for a POD of 100 mg/m$^3$ derived from an animal study in which animals are exposed by inhalation for 6 hours per day, 5 days per week, the adjustment to a continuous exposure concentration would consider both hours per day and days per week:

$$100\ mg/m^3 \times \frac{6}{24} \times \frac{5}{7} = 18\ mg/m^3 \qquad \text{(Equation 5-1)}$$

Thus, 18 mg/m$^3$ is the POD concentration adjusted for continuous exposure versus 100 mg/m$^3$ unadjusted. This approach assumes there is no dose-rate effect (i.e., that the same total inhaled material produces the same effect regardless of the time over which this material was inhaled).

Exposures documented from human occupational epidemiological studies are most often reported as 8-hr time-weighted averages (TWAs) and therefore, also are discontinuous. Adjustment of these exposures is usually done as part of the dosimetric adjustment to derive a human equivalent concentration (HEC), rather than as a discrete step, and is explained below in Section 5.6.3. The duration adjustment step also is explicitly incorporated into physiologically based pharmacokinetic (PBPK) models used to extrapolate an animal or occupational study-derived POD into an HEC.

After duration adjustment, the POD is converted into a **human equivalent concentration (HEC)** from the experimental animal dose. This conversion may be done using default methods specific to the particular chemical class of concern or more refined methods such as PBPK modeling.

The Agency's inhalation dosimetry methodology[6] provides a recommended hierarchy, as well as default generalized procedures for deriving **dosimetric adjustment factors** (**DAFs**) for this extrapolation. Application of DAFs to an animal exposure value yields an estimate of the corresponding concentration relevant to humans (i.e., the HEC) given differences in physiology and in the form of the pollutant that influence how the chemical exerts its effect. The DAF depends on the chemical category (i.e., gas or particle) and whether the adverse effect occurs in the respiratory tract or outside of the respiratory tract. HECs are derived using DAFs for both RfC development (noncancer effects) and IUR development (cancer).

When data are adequate to support it, the preferred EPA approach for calculating a HEC is to use a chemical-specific PBPK model parameterized for the animal species and regions (e.g., of the respiratory tract) involved in the toxicity (Exhibit 5-17).

In PBPK models, the body is subdivided into a series of anatomical or physiological "compartments" that represent specific organs or tissue and organ groups. The transfer of chemicals between compartments is described by a set of differential equations. The parameters of the model are of three types: physiological parameters (such as tissue perfusions or tissue volumes), physicochemical parameters (such as partition coefficients that describe the degree of partitioning of a given chemical to a given tissue), and biochemical parameters describing metabolic processes. The structure of a PBPK model is determined by the intended use of the model, the biochemical properties of the chemical studied, and the effect site of concern.

**Choice of a Default DAF for Extrapolation from Animal Data Depends on the Physical and Chemical Properties of the Pollutant**

**Gases**

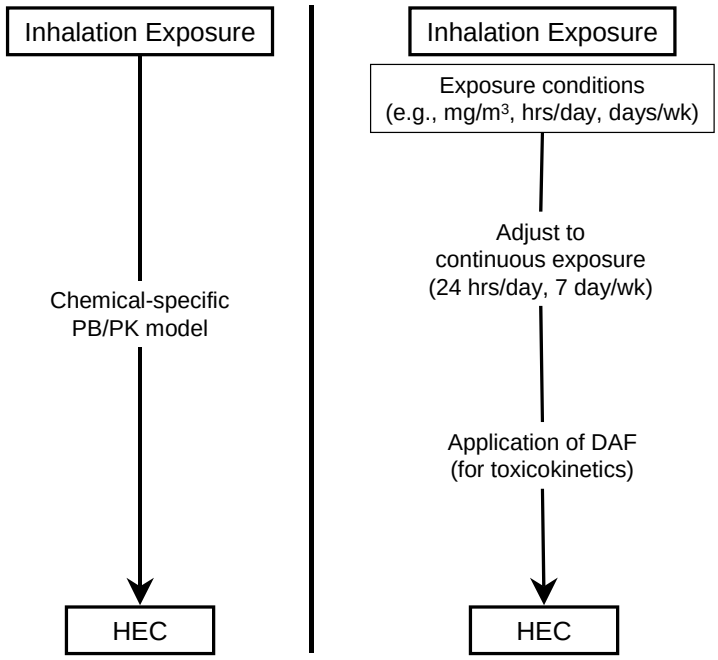
- Category 1 (effect in respiratory system) – default DAF based on inhalation rate, and surface area of target portion of respiratory tract
- Category 2 (some characteristics intermediate or common to category 1&3) – default DAF is the more restrictive of the defaults for category 1 & 3
- Category 3 (systemic effect[s]) – default DAF based on blood:air partition coefficient

**Particles**

- Respiratory toxicant – default DAF based on fractional deposition, inhalation rate, and surface area of target portion of respiratory tract
- Systemic toxicant – default DAF based on inhalation rate, body weight, and fractional deposition

*Source*: U.S. EPA. 1994. *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*.[6]

**Exhibit 5-17. Extrapolation of Inhalation Exposure to Calculate the HEC**




EPA employs a hierarchy of approaches for deriving the human equivalent concentration. Preference is given to the use of a physiologically-based pharmacokinetic model, followed by intermediate, less detailed approaches, which are followed by the default approach, which utilizes a DAF specific to the type of chemical and how it exerts its effect.

With sufficient data, a PBPK model is capable of calculating internal doses to a target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same internal dose (i.e., the HEC). A formal DAF is not calculated in this process; rather, the model itself serves as a DAF in estimating HECs. However, constructing a PBPK model is an information-intensive process, requiring much chemical-specific data. Consequently, these models are usually available for only a subset of chemicals. For example, EPA's IRIS toxicity assessment for vinyl chloride relies on a PBPK model.

#### 5.4.4.3 Extrapolation from POD to Derive Carcinogenic Potency Estimates

Observable cancer rates in laboratory or human occupational epidemiologic studies tend to be several orders of magnitude higher than cancer risk levels that society is willing to tolerate from involuntary chemical exposures. To obtain observable results, laboratory studies need to be conducted at exposures usually well above environmentally relevant concentrations. Thus, extrapolation from the POD-HEC to lower doses is usually necessary. This extrapolation is performed consistent with the mode of action, if adequately supported. Where the mode of action supports a biologically-based model and the data set is not rich enough to support a biologically based model, a non-linear reference concentration approach is employed (see Section 5.7.2). When the data are insufficient to support a mode of action decision, or where the data support a linear mode of action, a linear extrapolation is employed.

For linear extrapolation, a straight line is drawn from the point of departure expressed as a human equivalent dose to the origin (i.e., zero incremental dose, zero incremental response) to give an incremental probability dose unit. That is, the slope of the line expresses extra risk per dose unit (e.g., the IUR, expressed as extra risk per $\mu g/m^3$ of lifetime exposure). EPA's 1999 proposed guidelines[5] for carcinogen risk assessment recommend the use of the lowest effective dose using a 10 percent response level ($LED_{10}$) (as estimated by the lower one-sided confidence limit on the benchmark concentration [or $BMCL_{10}$]) as the POD for linear extrapolation. This approach is to draw a straight line between the estimated point of departure, generally, as a default, the $LED_{10}$. The $LED_{10}$ is the lower 95 percent limit on a dose that is estimated to cause a 10 percent response. The linear extrapolation approach to assessing risk is considered generally conservative of public health, including sensitive subpopulations, in the absence of specific information about the extent of human variability in sensitivity to effects.

The inhalation cancer dose-response value derived by linear extrapolation is the IUR. It is presented as an upper-bound estimate of the excess cancer risk resulting from a lifetime (assumed 70-year) of continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air. As illustrated previously in Exhibit 5-11A, risk is the product of the slope and the estimated exposure. The IUR is a plausible upper-bound estimate of the risk (i.e., the risk is not likely to be higher but may be lower and may be zero). When adequate human epidemiology data are available, maximum likelihood estimates may be used instead of upper bounds to generate the IUR. When only animal data are available and linear extrapolation is used, the IUR is derived from the largest linear slope that is consistent with the data (within the upper 95 percent confidence limit). In other words, the true risk to humans, while not identifiable, is not likely to exceed the upper-bound estimate (the IUR), and is likely to be lower. This means that any estimate of risk for air toxics using an IUR is likely to be protective of all potentially exposed populations. In addition, this means that air toxics risk estimates are likely to be conservative, that is, protective of public health.

Risk = EC × IUR, where

| | | |
|---|---|---|
| EC | = | lifetime estimate of continuous inhalation exposure to an individual air toxic |
| IUR | = | the corresponding inhalation unit risk estimate for that air toxic |

The evidence for the carcinogenic mode of action may lead to a conclusion that the dose-response relationship is nonlinear, with response falling much more quickly than linearly with dose, or may be most influenced by individual differences in sensitivity. In some cases this may be due to the mode of carcinogenic action being a secondary effect of toxicity or of an induced physiological change that is itself a threshold phenomenon. EPA does not generally try to distinguish between modes of action that might imply a "true threshold" from those with a nonlinear dose-response relationship. Except in unusual cases where extensive information is available, it is not possible to distinguish between these empirically. Therefore, as a matter of science policy, nonlinear probability functions are only fitted to the response data to extrapolate quantitative low-dose risk estimates when the carcinogenic mechanism of the toxicant is very well-understood. When the evidence indicates a non-linear dose response function containing a significant change in slope, and alternate nonlinear approach may be considered. For example, when carcinogenesis can be shown to be a secondary effect of threshold toxicity, the EPA *2005 Cancer Guidelines* recommend derivation of a reference concentration.

### 5.4.5 Dose-Response Assessment for Derivation of a Reference Concentration

The reference concentration is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive sub-populations) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfC is expressed as a chronic exposure level to the chemical in ambient air (in units of milligrams of the substance per cubic meter of air, or $mg/m^3$). This value is usually derived for use with effects other than cancer. But when a chemical's carcinogenicity has been shown to be associated with a nonlinear mode of action (see Agency's Cancer Guidelines),[5] a reference concentration may be derived for use with all effects, including cancer.

Inherent in the derivation of a reference concentration is the recognition of an exposure level likely to be without an appreciable risk of adverse effects (e.g., a sub-threshold level for adverse effects). The objective of this type of dose-response assessment, then, is to estimate that exposure level for humans. The RfC is derived after a thorough review of the health effects database for an individual chemical and identification of the most sensitive and relevant endpoint (the "critical effect") along with the principal study(ies) demonstrating that endpoint. In addition to an analysis of the study data available for the chemical, risk assessors also use uncertainty factors to account for differences in sensitivity between humans and laboratory animals, the possibility of heightened sensitivity of some population groups (e.g., people with respiratory disease, very young children, the aged), and any limitations of the database. The methodology for derivation of an inhalation reference concentration is described in detail in EPA's *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*.[6]

The first part of this type of assessment, which involves a careful qualitative and quantitative analysis of the study data, parallels that performed for linear cancer dose-response assessment (i.e., derivation of the point of departure in terms of a human equivalent concentration [$POD_{HEC}$]). The qualitative analysis is described in Section 5.5.2, while the quantitative analysis is described in Sections 5.6.1 and 5.6.2. The latter part of this type of assessment involves the application of uncertainty factors to address limitations of the data used (e.g., the factors raised above).

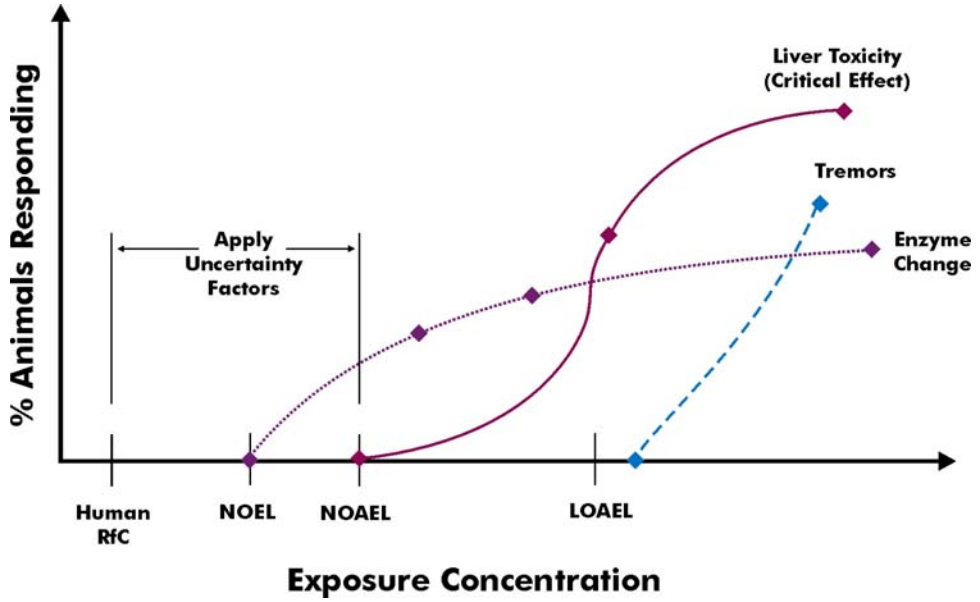
In IRIS, EPA includes with each RfC a statement of high, medium, or low confidence based on the completeness of the database for that substance. High confidence RfCs are considered less likely to change substantially with the collection of additional information, while low confidence RfCs may be especially vulnerable to change.[6]

#### 5.4.5.1 Determination of the Point of Departure and Human Equivalent Concentration

In earlier sections (Section 5.5.2, 5.6.1 and 5.6.2) the analysis of the database and identification of the critical effect, as well as the derivation of the POD in terms of human equivalent concentrations are discussed.

In developing a dose-response assessment, toxicologists evaluate the available data for a substance. Studies of high quality are selected, and the assessment is focused on the most appropriate studies. As the RfC is a chronic value, preference is given to long-term studies over short-term ones, to studies using animals that exhibit effects similar to those experienced by humans, to studies using an appropriate exposure route (e.g., inhalation exposure for developing an RfC), and to studies showing a clear pattern of increasing frequency or severity of response with increasing dose. Toxicologists use the information to identify the **critical effect** (i.e., the adverse effect that appears at the lowest dose). Afterwards, appropriate human data are chosen as the basis for the RfC or, if human data are not adequate, data from the most appropriate species are identified. If this is not known, the data from the most sensitive species is usually chosen. This analysis is described in Section 5.5.2. The objective in identifying the critical effect or effects is to identify the effect(s) - among all those associated with exposure to the chemical of interest - that occur at the lowest exposure and would lead to derivation of the lowest RfC (Exhibit 5-18).

**Exhibit 5-18. Overview to Develop a Reference Concentration**




The LOAEL (HEC) and NOAEL (HEC) are illustrated with low-dose extrapolation with the application of uncertainty or modifying factors to derive the human health-protective RfC. Note that this figure represents data from appropriate animal species.

Using the dose-response relationship for the critical effect, toxicologists identify the POD from the experimental data. This exposure concentration (in terms of its human equivalent) which marks the boundary between the range of observation and that of extrapolation, is the point from which extrapolation begins for derivation of a RfC. The POD may be derived from benchmark modeling (see Section 5.6.1 regarding the derivation of a BMCL). If the data do not meet requirements for benchmark modeling, the POD is derived by the use of a statistical analysis to identify the **no-observed-adverse-effect-level**, or **NOAEL**, defined as the highest dose level administered to laboratory animals that did not cause statistically or biologically significant observable adverse effects after chronic (usually lifetime) exposure in the studied population. In some cases, a LOAEL is used in the absence of a NOAEL. In either case, the POD is transformed into a continuous inhalation exposure (e.g., from an intermittent animal exposure, 6 hours/day, 5 days/week) and then into a human equivalent concentration (as described in Section 5.6.2). In order for the appropriate critical effect to be identified, a comparison of PODs across different endpoints is done in terms of human equivalent concentrations (or potential RfC values, which incorporate the application of UFs, need to be compared).[6]

**Derivation of RfC Using BMC Methodology – 1,3-Dichloropropene**

A review of the available animal studies indicated changes to the surface cells of the nasal portion of the respiratory tract as the critical effect for 1,3-dichloropropene. Benchmark modeling was performed on the data demonstrating this effect. The seven statistical models for dichotomous data from the Agency's benchmark dose modeling software (BMDS Version.1b) were applied to the incidence data for the adjusted administered doses. The best model fit was determined by eliminating all models that did not have a statistically significant goodness-of-fit ($p<0.05$). The remaining models were then ranked by best visual fit of the data, especially for the lower doses, as observed in the graphical output of the Benchmark Dose Software. The model with statistically significant goodness-of-fit and best visual and statistical fit was used to estimate the BMC at 10 percent risk and the 95 percent lower confidence limit of the BMC (the BMCL). The gamma, logistic, multistage, Weibull, and quantal-quadratic models provided statistically significant fits. The gamma model was the best fit overall because it provided the best visual fit. This model yielded a $BMC_{10}$ of 5.9 mg/m$^3$ and a $BMCL_{10}$ of 3.7 mg/m$^3$.

The $BMCL_{10}$ was identified as the POD and was adjusted from experimental conditions to a continuous inhalation exposure value ($POD_{adj}$). Because the critical target was the nasal mucosa, algorithms for extrathoracic effects for Category 1 gases were used to adjust continuous animal exposure concentration to HEC. The $POD_{HEC}$ for a Category 1 gas was derived by multiplying the animal $BMCL_{10}$ by an interspecies dosimetric adjustment for gas:respiratory effects in the extrathoracic area of the respiratory tract. Using default values, the adjustment factor was equal to 0.2. For example, for 1,3-dichloropropene:

$$POD_{HEC} = BMCL_{10}(HEC) = BMCL_{10}\ (adj) \times 0.2 = 3.7 \times 0.2 = 0.7\ mg/m^3$$

The $POD_{HEC}$ was divided by uncertainty factors for interspecies extrapolation (UF of 3) and intraspecies variation (UF of 10) and rounded to one significant figure to yield the RfC for 1,3-dichloropropene:

$$RfC = POD_{HEC} / 30 = 0.02\ mg/m^3$$

#### 5.4.5.2 Application of Uncertainty Factors

The RfC is an estimate derived from the $POD_{HEC}$ for the critical effect (based on either a $BMCL_{HEC}$, $NOAEL_{HEC}$ or $LOAEL_{HEC}$) by consistent application of UFs. The UFs are applied to account for recognized uncertainties in the use of the available data to estimate an exposure concentration appropriate to the assumed human scenario. The general formula for deriving an RfC from a $POD_{HEC}$ is:

$$RfC\,(mg/m^3) = \frac{POD_{HEC}(mg/m^3)}{UF} \qquad \text{(Equation 5-2)}$$

A UF of 10, 3, or 1 is applied for each of the following extrapolations used to derive the RfC (see Exhibit 5-19):

- Animal to human;
- Human to sensitive human populations;
- Subchronic to chronic;
- LOAEL to NOAEL; and
- Incomplete to complete database.

The UFs are generally an order of magnitude (10), although incorporation of dosimetry adjustments or other information may result in the use of reduced UFs for RfCs (3 or 1). The composite UF applied to an RfC will vary in magnitude depending on the number of uncertainties involved; however, an RfC will not be derived when use of the data involves more than four areas of extrapolation. The composite UF when four factors are used generally is reduced from 10,000 to 3,000 in recognition of the lack of independence and the conservatism of these factors.

The 2002 Agency review of the reference dose (RfD)/reference concentration process[3] encouraged the development of guidance in the area of chemical-specific adjustment factors (CSAFs). These factors utilize specific data to replace the default UFs for interspecies or inter-individual variation. The review panel noted, however, that the CSAF approach for any single substance is determined principally by the availability of relevant data. For many substances there are relatively few data available to serve as an adequate basis to replace defaults for interspecies differences and human variability with more informative CSAFs.

| Exhibit 5-19. Uncertainty Factors Used in the Derivation of an Inhalation RfC | |
|---|---|
| **Standard Uncertainty Factors** | **Processes Considered in UF Purview** |
| **A = Animal to human**<br>Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans. | • Pharmacokinetics/Pharmacodynamics<br>• Relevance of laboratory animal model<br>• Species sensitivity |
| **H = Human to sensitive human**<br>Extrapolation of valid experimental results for studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population. | • Pharmacokinetics/Pharmacodynamics<br>• Sensitivity<br>• Differences in mass (children, obese)<br>• Concomitant exposures<br>• Activity Pattern<br>• Does not account for idiosyncrasies |
| **S = Subchronic to chronic**<br>Extrapolation from less than chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs. | • Accumulation/Cumulative damage<br>• Pharmacokinetics/Pharmacodynamics<br>• Severity of effect<br>• Recovery<br>• Duration of study<br>• Consistency of effect with duration |
| **L = LOAEL to NOAEL**<br>Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs. | • Severity<br>• Pharmacokinetics/Pharmacodynamics<br>• Slope of dose-response curve<br>• Trend, consistency of effect<br>• Relationship of endpoints<br>• Functional vs histopathological evidence<br>• Exposure uncertainties |
| **D = Incomplete to complete data**<br>Extrapolation from valid results in laboratory animals when the data are "incomplete". Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans. | • Quality of critical study<br>• Data gaps<br>• Power of critical study/supporting studies<br>• Exposure uncertainties |
| *Source*: U.S. EPA. 1994. *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*.[6] | |

Because of this procedure to address the lack of information on the translation from experimental data to a human scenario, the resulting RfC for many HAPs is on the order of 100 to 300 times lower than the NOAEL actually observed in the animal testing (see Exhibit 5-20). This reflects the lowering of the RfC to address the uncertainties in the extrapolations mentioned above. For those HAPs that have had their effects well documented in human studies, the RfC may be much closer to the highest concentration at which an adverse effect was not observed (e.g., within a factor of 3 to 10).

| Exhibit 5-20. Examples of the Use of Uncertainty Factors in Deriving RfCs | |
|---|---|
| **RfC from NOAEL**<br>**Example: Diesel Engine Emissions** | **RfC from LOAEL**<br>**Example: Toluene** |
| *Toxicity data:*<br>144 µg chemical/$m^3$ air ($NOAEL_{HEC}$ from chronic rodent study)<br><br>*Uncertainty factors*: 3 x 10 = 30<br><br>3 = animal-to-human extrapolation<br>10 = human to sensitive human subpopulations<br><br>RfC = 144/30 = 4.8 µg/$m^3$ = 0.005 mg/$m^3$ | *Toxicity data:*<br>119 mg chemical/$m^3$ air ($LOAEL_{HEC}$ from chronic occupational study)<br><br>*Uncertainty factors*: 10 x 10 x 3 = 300<br><br>10 = human to sensitive human subpopulations<br>10 = LOAEL-to-NOAEL extrapolation<br>3 = database deficiencies<br><br>RfC = 119/300 mg/$m^3$ = 0.4 mg/$m^3$ |
| $NOAEL_{HEC}$ = No-Observed-Adverse-Effect Level (Human Equivalent Concentration)<br>$LOAEL_{HEC}$ = Lowest-Observed-Adverse-Effect Level (Human Equivalent Concentration)<br><br>*Source*: EPA's IRIS database http://www.epa.gov/IRIS/. | |

In some of the older IRIS assessments a "modifying factor" may have been applied in addition to the traditional uncertainty factors. It had been used with professional judgement when it was determined that another uncertainty factor was needed; its magnitude depended upon the professional assessment of scientific uncertainties of the study and database not explicitly treated via the other uncertainty factors.[(6)] The 2002 Agency review of the RfD/RfC process, however, recommended against continued use of the modifying factor. It was felt that the traditional factors could account for any remaining uncertainties.[(3)]

### 5.4.6 Sources of Chronic Dose-Response Values

Appendix C of ATRA, Volume 1 provides a current listing of appropriate chronic dose-response values (i.e., RfCs or comparable values and IURs) for HAPs.[(p)] References for acute exposure levels are provided below in Exhibit 5-21. Hazard identification and dose-response assessment information for chronic exposure (presented in ATRA Volume 1, Appendix C), was obtained from various sources and prioritized according to (1) conceptual consistency with EPA risk assessment guidelines, and (2) level of review received. The prioritization process was aimed at incorporating into our assessments the best available science with respect to dose-response information. The sources listed below were used, and provide this information for chemicals beyond the 187 Clean Air Act hazardous air pollutants listed in Appendix C of ATRA Volume 1.

- **U.S. Environmental Protection Agency (EPA)**. EPA has developed dose-response assessments for chronic exposure to many pollutants. These assessments typically specify an RfC (to protect against effects other than cancer) and/or IUR (to estimate the probability of contracting cancer). Background documents, particularly for the more recent files, also contain information on physical and chemical properties, toxicokinetics, and hazard

[p] As noted earlier, see http://www.epa.gov/ttn/atw/toxsource/summary.html for a current listing of this information.

characterization. EPA disseminates dose-response assessment information in several forms, based on the level of review. Dose-response assessments that have achieved full intra-agency consensus are incorporated in the **Integrated Risk Information System (IRIS)**, which is regularly updated and available on-line (www.epa.gov/iris). All IRIS assessments since 1996 also have undergone independent external peer review. In the past, dose-response assessments for some substances were prepared by the EPA Office of Research and Development, but were never submitted for EPA consensus. EPA has assembled the results of many such assessments in the **Health Effects Assessment Summary Tables (HEAST)**. Although the values in HEAST have undergone some review and have the concurrence of individual Agency program offices, they have not had enough review to be recognized as Agency-wide consensus information. In addition, since HEAST has not been updated since 1997, other sources described here are, for many chemicals, more reliable.

- **Agency for Toxic Substances and Disease Registry (ATSDR)**. ATSDR, which is part of the US Department of Health and Human Services, develops and publishes Minimum Risk Levels (MRLs) for many toxic substances. The MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (other than cancer) over a specified duration of exposure. MRLs are derived for acute (1-14 days), intermediate (>14-364 days), and chronic (365 days and longer) exposures by inhalation and oral routes. ATSDR describes MRLs as substance-specific estimates to be used by health assessors to select environmental contaminants for further evaluation. MRLs are presented with only one significant figure and are considered to be levels below which contaminants are unlikely to pose a health threat. Exposures above an MRL do not necessarily represent a threat, and MRLs are therefore not intended for use as predictors of adverse health effects or for setting cleanup levels. The MRL data undergo a rigorous review process, including internal ATSDR review, peer reviews, and public comment periods. ATRA Volume 1, Appendix C shows the ATSDR chronic MRL where no IRIS value is available, because the MRL's concept, definition, and derivation are philosophically consistent (though not identical) with EPA's guidelines for assessing noncancer effects. ATSDR publishes MRLs as part of pollutant-specific toxicological profile documents, and also in regularly-updated on-line tables.[8]

- **California Environmental Protection Agency (CalEPA)**. The CalEPA Office of Environmental Health Hazard Assessment (OEHHA) has developed dose-response assessments for many substances, based both on carcinogenicity and health effects other than cancer. The process for developing these assessments is similar to that used by EPA to develop IRIS values and includes significant external scientific peer review. The non-cancer information includes inhalation health risk guidance values expressed as chronic inhalation reference exposure levels (RELs). CalEPA defines the REL as a concentration level at (or below) which no health effects are anticipated, a concept that is substantially similar to EPA's approach to non-cancer dose-response assessment. ATRA Volume 1, Appendix C shows the chronic REL (including both final and proposed values) where no IRIS RfC/RfD or ATSDR MRL exists. CalEPA's quantitative dose-response information on carcinogenicity by inhalation exposure is expressed in terms of the IUR, defined similarly to EPA's IUR. ATRA Volume 1, Appendix C shows specific CalEPA UREs where no IRIS values exist. CalEPA's dose response assessments for carcinogens and noncarcinogens are available on-line.[9]

- **International Agency for Research on Cancer** (**IARC**). The IARC, a branch of the World Health Organization, coordinates and conducts research on the causes of human cancer and develops scientific strategies for cancer control. The IARC sponsors both epidemiological and laboratory research, and disseminates scientific information through meetings, publications, courses and fellowships. As part of its mission, the IARC assembles evidence that substances cause cancer in humans and issues judgments on the strength of evidence. IARC's categories are Group 1 (carcinogenic in humans), Group 2A (probably carcinogenic), Group 2B (possibly carcinogenic), Group 3 (not classifiable), and Group 4 (probably not carcinogenic). The categorization scheme may be applied to either single chemicals or mixtures; however, IARC does not develop quantitative dose-response metrics such as UREs,. IARC's categories for substances are included in ATRA Volume 1, Appendix C to support or augment EPA's weight-of evidence (WOE) determinations, which do not cover all substances and in some cases may be out-of-date. The list of IARC evaluations to date is available on-line (http://193.51.164.11/monoeval/grlist.html).

Additionally, the EPA has compiled fact sheets for the 187 CAA hazardous air pollutants and makes them available on the Air Toxics website (http://www.epa.gov/ttn/atw/hapindex.html). This collection is called the **Health Effects Notebook for Hazardous Air Pollutants**, and provides for each HAP a summary of available information in the following categories: hazard summary, physical properties, uses, sources and potential exposure, and health hazard information. These fact sheets are useful for describing hazards associated with the 187 HAPs.

### 5.4.7 Acute Exposure Reference Values

Many air pollutants can cause adverse health effects after acute or short-term exposures lasting from a few minutes to several days. For some pollutants, acute exposures may be of greater concern than chronic exposures. The severity of effects from acute exposures may vary widely. Agency-wide guidance on how to assess toxic effects from short-term exposures is currently being developed. This guidance for Acute Reference Exposure (ARE) levels is intended to assist acute risk assessment activities. A variety of other short-term, acute exposure limits are also described in Exhibit 5-21.[10] ATRA Volume 1, Appendix C provides a current listing of acute dose-response values for HAPs.

Methods for dose-response assessment of acute exposures are usually similar to the approach for chronic exposure, with their derivation involving the identification of a "critical effect," determination of a NOAEL or comparable value for that effect, and application of uncertainty factors (e.g., animal to human population). However, the process by which most acute inhalation dose-response assessment values are derived differs from the chronic RfC methodology in two important ways. First, "acute" may connote exposure times varying from a few minutes to two weeks. The time frame for the value is critical, because the safe dose (or the dose that produces some defined effect) may vary substantially with the length of exposure. Second, some acute dose-response assessments include more than one level of severity. A typical assessment may have values for level 1 (at which only mild, transient effects may occur), level 2 (above which irreversible or other serious effects may occur), and level 3 (above which life-threatening effects may occur). Therefore, many acute assessments present dose-response assessment values as a matrix, with one dimension being length of exposure and the other a severity-of-effect category.

| Exhibit 5-21. Examples of Available Short-Term, Acute Exposure Levels | | | | |
|---|---|---|---|---|
| **Acronym** | **Full Name** | **Group or Agency** | **Purpose/Definition** | **Source/Website** |
| **AEGL** | Acute Exposure Guideline Level | National Research Council (NRC) National Advisory Committee (NAC) | The AEGLs represent short-term threshold or ceiling exposure values intended for the protection of the general public, including susceptible or sensitive individuals, but not hypersusceptible or hypersensitive individuals. The AEGLs represent biological reference values for this defined human population and consist of three biological endpoints for four different single emergency (accidental) exposure periods (30 minutes, l hour, 4 hours, and 8 hours). In some instances, AEGLs also are developed for 5 or 10 minutes. The biological endpoints are defined as follows:<br>• AEGL-1 is the airborne concentration (expressed as parts per millions [ppm] or milligrams [mg]/meters [m]$^3$) of a substance at or above which it is predicted that the general population, including "susceptible" but excluding "hypersusceptible" individuals, could experience notable discomfort. Airborne concentrations below AEGL-1 represent exposure levels that could produce mild odor, taste, or other sensory irritations.<br>• AEGL-2 is the airborne concentration (expressed as ppm or mg/m$^3$) of a substance at or above which it is predicted that the general population, including "susceptible" but excluding "hypersusceptible" individuals, could experience irreversible or other serious, long-lasting effects or impaired ability to escape. Airborne concentrations below the AEGL-2 but at or above AEGL-1 represent exposure levels that may cause notable discomfort.<br>• AEGL-3 is the airborne concentration (expressed as ppm or mg/m$^3$) of a substance at or above which it is predicted that the general population, including "susceptible" but excluding "hypersusceptible" individuals, could experience life-threatening effects or death. Airborne concentrations below AEGL-3 but at or above AEGL-2 represent exposure levels that may cause irreversible or other serious, long-lasting effects or impaired ability to escape. | http://search.nap.edu/books/0309072948/html/ |
| **ARE** | Acute Reference Exposure | U.S. Environmental Protection Agency | The ARE is an informed estimate of the highest inhalation exposure (concentration and duration) that is not likely to cause adverse effects in a human population, including sensitive subgroups, exposed to that scenario, even on an intermittent basis.[11] For these purposes, acute exposures are single continuous exposures lasting 24 hours or less; AREs may be derived for any duration of interest within that period. "Intermittent" implies sufficient time between exposures such that one exposure has no effect on the health outcome produced by the next exposure. EPA is in the process of finalizing the methodology for development of AREs. | |

| Exhibit 5-21. Examples of Available Short-Term, Acute Exposure Levels | | | | |
|---|---|---|---|---|
| **Acronym** | **Full Name** | **Group or Agency** | **Purpose/Definition** | **Source/Website** |
| **BEI** | Biological Exposure Indices | American Conference of Governmental Industrial Hygenists | BEIs® are health-based values for use by industrial hygienists in making decisions regarding safe levels of exposure to various chemical and physical agents found in the workplace. | http://www.acgih.org/TLV/ |
| **CEEL** | Community Emergency Exposure Level | National Research Council (NRC) National Advisory Committee (NAC) | CEELs are ceiling exposure values for the public applicable to emergency exposures of foreseeable magnitude and duration, usually not exceeding 1 hour. Three CEELs were established:<br>• CEEL-1: Concentration above which discomfort, for example eye and nose irritation or headaches, becomes increasingly common;<br>• CEEL-2: Concentration above which disability, for example, severe eye or respiratory irritation, becomes increasingly common;<br>• CEEL-3: Concentration above which death or life-threatening effects, for example, pulmonary edema, cardiac failure, or cancer, become increasingly common. | Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances (NRC, 1993) |
| **EEGL** | Emergency Exposure Guidance Level | NAS Committee on Toxicology | Exposure levels judged to be acceptable for military personnel performing tasks during emergency situations. Not considered safe exposure level for routine or normal operations. | |
| **ERPG** | Emergency Response Planning Guideline | American Industrial Hygiene Association's (AIHA) Emergency Response Planning Committee | These guidelines are intended for application by persons trained in emergency response planning.<br>ERG-1: The maximum concentration in air below which it is believed nearly all individuals could be exposed for up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor.<br>ERG-2: The maximum concentration in air below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair their abilities to take protective action.<br>ERG-3: The maximum concentration in air below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects. | http://www.bnl.gov/scapa/erpgpref.htm<br><br>http://www.bnl.gov/scapa/scapawl.htm |
| **IDLH** | Immediately Dangerous to Life or Health Concentration | National Institute for Occupational Safety and Health (NIOSH) | An immediately dangerous to life or health condition is one "that poses a threat of exposure to airborne contaminants when that exposure is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from such an environment. The purpose of establishing an IDLH is to ensure that the worker can escape from a given contaminated environment in the event of failure of the respiratory protection equipment. | NIOSH Respirator Decision Logic [NIOSH 1987],<br><br>http://www.cdc.gov/niosh/idlh/intridl4.html |

| Exhibit 5-21. Examples of Available Short-Term, Acute Exposure Levels | | | | |
|---|---|---|---|---|
| **Acronym** | **Full Name** | **Group or Agency** | **Purpose/Definition** | **Source/Website** |
| **LOC** | Level of Concern | U.S. Environmental Protection Agency, Federal Emergency Management Agency, U.S. Department of Transportation | Defined by the Technical Guidance for Hazards Analysis (a guide developed to assist in planning for accidental chemical releases). As the concentration of an extremely hazardous substances in air above which there may be serious irreversible health effects or death as a result of a single exposure for a relatively short period of time. In the 1987 Technical Guidance for Hazards Analysis document, an LOC was estimated by using one-tenth of the IDLH level published by the National Institute for Occupational Safety and Health. For the purposes of offsite consequence analysis performed as part of accidental release requirements under Section 112®) of the CAA, this value is superceded by ERPG-2 values as available, and the Agency intends to supercede those values with AEGL-2 values as they are developed and adopted. | Technical Guidance for Hazards Analysis. Emergency Planning for Extremely Hazardous Substances. (USEPA, FEMA, USDOT, 1987). 61 FR 31672; June 20, 1996 |
| **MRL** | Acute Minimum Risk Levels | U.S. Agency for Toxic Substances and Disease Registry (ATSDR) | The MRL is an estimate of human exposure to a substance that is likely to be without an appreciable risk of adverse effects (other than cancer) over a specified duration of exposure, and can be derived for acute exposures by the inhalation and oral routes. Unlike the one-hour focus of most of the other values listed here, acute MRLs are derived for exposures of 1 to 14 days duration. | http://www.atsdr.cdc.gov/mrls.html |
| **REL** | Reference Exposure Level | California EPA Office of Environmental Health Hazard Assessment (OEHHA) | The acute REL is an exposure that is not likely to cause adverse effects in a human population, including sensitive sub-populations, exposed to that concentration for one hour on an intermittent basis. RELs are based on the most sensitive, relevant, adverse health effect reported in the medical and toxicological literature. RELs are designed to protect the most sensitive individuals in the population by the inclusion of margins of safety. Since margins of safety are incorporated to address data gaps and uncertainties, exceeding the REL does not automatically indicate an adverse health impact OEHHA has defined the lowest available acute severity level as the REL. | http://www.oehha.ca.gov/air/pdf/acuterel.pdf |
| **SPEGL** | Short-term Public Emergency Exposure Guidance Level | National Academy of Sciences (NAS) Committee on Toxicology | The NAS develops short-term public emergency exposure guidance levels (SPEGLs) to apply to the exposures of the general public to contaminants during airborne chemical releases; SPEGLs are generally set at a level of 0.1 to 0.5 times the EEGL and are measured as 60 minute or 8 hour exposure time frames. | *Criteria and Methods for Preparing Emergency Exposure Guidance Level (EEGL), Short-Term Public Emergency Guidance Level (SPEGL), and Continuous Exposure Guidance Level (CEGL) Documents.* 1986. National Academy Press, National Academy of Sciences ,Washington, D.C. |

| Exhibit 5-21. Examples of Available Short-Term, Acute Exposure Levels | | | | |
|---|---|---|---|---|
| **Acronym** | **Full Name** | **Group or Agency** | **Purpose/Definition** | **Source/Website** |
| **STEL** | Short-Term Exposure Limit | American Conference of Governmental Industrial Hygenists (ACGIH) | STELs are time weighted average (TWA) guidelines for the control of short term exposure in the workplace. These are important supplements to the eight-hour TWA exposure standards which are more concerned with the total intake over long periods of time. Generally, STELs are established to minimize the risk of the occurrence in nearly all workers of: intolerable irritation; chronic or irreversible tissue change; and narcosis to an extent that could precipitate industrial accidents, provided the eight hour TWA exposure standards are not exceeded. STELs are recommended for those substances only when there is evidence either from human or animal studies that adverse health effects can be caused by high short term exposure. STELs are expressed as airborne concentrations of substances, averaged over a period of 15 minutes. | |

### 5.4.8 Evaluating Chemicals Lacking Health Reference Values

#### 5.4.8.1 Use of Available Data Sources

If EPA-derived IRIS assessments are available for the chemicals being examined, these values should generally be used in the risk assessment. Use of IRIS or other EPA-derived dose-response values prevents duplication of effort in toxicity assessment and ensures consistency in the dose-response values among risk assessments. If EPA-derived dose-response values are not available, the other sources described in Section 5.9 should be given next priority. Use of these sources in a hierarchical manner has been implemented in tables developed for the 187 hazardous air pollutants (see ATRA Volume 1, Appendix C and http://www.epa.gov/ttn/atw/toxsource/table1.pdf). The Toxicology Excellence for Risk Assessment (TERA) maintains a database of international dose-response values (see www.TERA.org/iter).

If those sources also lack inhalation dose-response values, then route-to-route extrapolation (discussed below) may be considered. This approach, however, may be quite detailed, and requires assistance from a professional toxicologist. If all sources and approaches have been researched, and no dose-response value is available, the assessor should describe the effects of the chemical qualitatively and discuss the implications of the absence of the chemical from the risk estimate in the uncertainty section of the risk assessment.

#### 5.4.8.2 Route-to-Route Extrapolation

For cases in which appropriate dose-response values are not available for the route of exposure being considered, but are available for another route, it may be possible to use route-to-route extrapolation. Route-to-route extrapolation is recommended only from oral to inhaled exposure and only for carcinogens. The ability to perform quantitative route-to-route extrapolation is critically dependent on the amount and type of data available. Regardless of the toxic endpoint being considered, a minimum of information is required to construct plausible dosimetry for the routes of interest. This information includes both the nature of the toxic effect and a description of the relationship between exposure and the toxic effect.

**Route to route extrapolations should only be done by qualified toxicologists.**

Data from other routes of exposure may be useful to derive an RfC (for carcinogens only; discussed below) only when respiratory tract effects and/or "first pass" effects can be ruled out. First pass effects are cases where metabolism takes place in the portal-of-entry tissues, prior to entry into the systemic circulation. The respiratory tract can exhibit a first-pass effect after inhalation. Unless the first-pass effect and dosimetry are adequately understood, there can be substantial error introduced in route-to-route extrapolation that does not account for these considerations.

Oral toxicity data should *not* be used for route-to-route extrapolation in the following cases (unless these effects can be accounted for in a PBPK model):

- When groups of chemicals have different toxicity by the two different routes (e.g., metals, irritants, and sensitizers);

- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract is not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for an RfC development.

The actual impact of exposure by different routes can only be estimated by taking account of factors that influence absorption at the portal of entry, such as (1) physicochemical characteristics of the chemical; (2) exposure factors; and (3) physiologic parameters. The preferred method for performing route-to-route extrapolation involves the development of a PBPK model that describes the disposition of the chemical for the routes of interest. As previously discussed, PBPK models account for fundamental physiologic and biochemical parameters and processes such as blood flow, ventilatory parameters, metabolic capacities, and renal clearance, tailored by the physicochemical and biochemical properties.

If appropriate toxicity information is not available, a qualitative rather than quantitative evaluation of the chemical is recommended. The implications of the absence of the chemical from the risk estimate should be discussed in the uncertainty section.

### 5.4.9 Dose-Response Assessment for Mixtures

The recommended approach for assessing risks from exposure to a mixture of pollutants (e.g., coke oven emissions, diesel exhaust, etc.) is to utilize a dose-response assessment developed for that mixture or a mixture judged similar.[12] [13] Where such an assessment is not available, a component-by-component approach may be employed. There are several commonly used approaches. Selection among the approaches involves consideration of the similarity of the mixture components with regard to their toxicological activity. There are a few groups of toxicologically similar chemicals for which the Agency recommends the use of relative potency factors (RPFs) or toxicity equivalence factors (TEFs). These factors have been developed by EPA and other organizations for two classes of compounds: PAHs and dioxins/furans. The World Health Organization (WHO) has developed TEFs for polychlorinated biphenyls (PCBs) as an extension of the factors for dioxins/furans (see Exhibit 5-22).

- **Polycyclic Aromatic Hydrocarbons (PAHs)**. EPA has not developed IURs or CSFs for carcinogenic PAHs other than benzo(a)pyrene. EPA recommends use of a RPF based on the potency of each compound relative to that of benzo(a)pyrene.[14] Although several references may be found in the literature with proposed RPFs for PAHs, EPA recommends the

following RPF values for seven PAHs, which are classified as B2, probable human carcinogens:[q]

| PAH | RPF |
|---|---|
| Benzo(a)pyrene | 1.0 |
| Benzo(a)anthracene | 0.1 |
| Benzo(b)fluoranthene | 0.1 |
| Benzo(k)fluoranthene | 0.01 |
| Chrysene | 0.001 |
| Dibenz(a,h)anthracene | 1.0 |
| Indeno(1,2,3-c,d)pyrene | 0.1 |

Thus, for these seven PAHs, the IUR for benzo(a)pyrene is multiplied by the applicable RPF to derive the IUR.

- **Dioxins, Furans, and PCBs**. For carcinogenic dioxins and furans, the TEF approach has an underlying assumption of additivity across mixture components. EPA currently recommends TEFs for specific congeners, rather than isomeric groups (see Exhibit 5-21). TEFs were determined by inspection of the available congener-specific data and an assignment of an "order of magnitude" estimate of relative toxicity when compared to 2,3,7,8-TCDD. The cancer potency of certain dioxin and furan congeners is estimated relative to 2,3,7,8-TCDD based on other toxicity information that is available for the congeners. Scientific judgment and expert opinion formed the basis for these TEF values. External review of the toxicity and pharmacokinetic data utilized in setting these TEF values supported the basic approach as a "reasonable estimate" of the relative toxicity of polychlorinated dibenzo-dioxins (PCDDs) and polychlorinated dibenzo-furans (PCDFs).[15] TEF values developed by scientific groups over the past 15 years are provided in Exhibit 5-21. The most recent consensus of the scientific community (including representation by EPA scientists) is represented by the WHO 1997 values.

  TEFs based on the relative cancer potencies are used to adjust the exposure concentrations of mixture components, which are subsequently summed into a single exposure concentration for the mixture. That exposure concentration based on TEFs is then used, along with the 2,3,7,8-TCDD IUR or noncancer reference value, to estimate cancer risks or other health hazards for the mixture.

[q] CalEPA has developed IURs based on RPFs for several additional PAHs that have been classified as probably or possibly human carcinogens (e.g., IARC).

| Exhibit 5-22. Toxicity Equivalence Factors for Dioxins, Furans and PCBs | | | | |
|---|---|---|---|---|
| **Congener** | **EPA (1987)[16]** | **NATO (1989)[17]** | **WHO (1994)[18]** | **WHO (1997)[19]** |
| **TCDDs** | | | | |
| 2,3,7,8-TCDD | 1 | 1 | | 1 |
| 1,2,3,7,8-PeCDD | 0.5 | 0.5 | | 1 |
| 1,2,3,4,5,8-HxCDD | 0.04 | 0.1 | | 0.1 |
| 1,2,3,7,8,9-HxCDD | 0.04 | 0.1 | | 0.1 |
| 1,2,3,6,7,8-HxCDD | 0.04 | 0.1 | | 0.1 |
| 1,2,3,4,6,7,8-HpCDD | 0.001 | 0.1 | | 0.01 |
| 1,2,3,4,6,7,8,9-OCDD | 0 | 0.001 | | 0.0001 |
| **TCDFs** | | | | |
| 2,3,7,8-TCDF | 0.1 | 0.1 | | 0.1 |
| 1,2,3,7,8-PeCDF | 0.1 | 0.05 | | 0.05 |
| 2,3,4,7,8-HxCDF | 0.1 | 0.5 | | 0.5 |
| 1,2,3,4,7,8-HxCDF | 0.01 | 0.1 | | 0.1 |
| 1,2,3,7,8,9-HxCDF | 0.01 | 0.1 | | 0.1 |
| 1,2,3,6,7,8-HxCDF | 0.01 | 0.1 | | 0.1 |
| 2,3,4,6,7,8-HxCDF | 0.01 | 0.1 | | 0.1 |
| 1,2,3,4,6,7,8-HpCDF | 0.001 | 0.01 | | 0.01 |
| 1,2,3,4,7,8,9-HpCDF | 0.001 | 0.01 | | 0.01 |
| 1,2,3,4,6,7,8,9-OCDF | 0 | 0.001 | | 0.0001 |
| **PCBs**<br>**IUPAC # Structure** | | | | |
| 77 3,3',4,4'-TCB | | | 0.0005 | 0.0001 |
| 81 3,4,4',5-TCB | | | – | 0.0001 |
| 105 2,3,3',4,4'-PeCB | | | 0.0001 | 0.0001 |
| 114 2,3,4,4',5-PeCB | | | 0.0005 | 0.0005 |
| 118 2,3',4,4',5-PeCB | | | 0.0001 | 0.0001 |
| 123 2',3,4,4',5-PeCB | | | 0.0001 | 0.0001 |
| 126 3,3',4,4',5-PeCB | | | 0.1 | 0.1 |
| 156 2,3,3'4,4',5-HxCB | | | 0.0005 | 0.0005 |
| 157 2,3,3',4,4',5'-HxCB | | | 0.0005 | 0.0005 |
| 167 2,3',4,4',5,5'-HxCB | | | 0.00001 | 0.00001 |
| 169 3,3'4,4'5,5'-HxCB | | | 0.01 | 0.01 |
| 170 2,2',3,3',4,4',5-HpCB | | | 0.0001 | – |
| 180 2,2',3,4,4',5,5'-HpCB | | | 0.00001 | – |
| 189 2,3,3',4,4',5,5'-HpCB | | | 0.0001 | 0.0001 |
| Source: EPA's dioxin reassessment activities[20] | | | | |

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