Integrated Risk Information System (IRIS)

The Integrated Risk Information System (IRIS) is a human health assessment program that evaluates quantitative and qualitative risk information on effects that may result from exposure to environmental contaminants. IRIS was initially developed for EPA staff in response to a growing demand for consistent information on substances for use in risk assessments, decision-making, and regulatory activities. The information in IRIS is intended for those without extensive training in toxicology, but with some knowledge of health sciences.

Getting Started with IRIS

- An overview of the web site
- What is IRIS?
- How does EPA decide which substances to add or update?

More frequent questions >>

Using the IRIS Database

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New Assessments and Reviews

The following documents are new assessments or under external Peer-Review at this time:
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Substance	Milestone	Meeting/Release date
Hexavalent Chromium	External Peer-Review Draft Interagency Science Discussion Draft	09/30/2010 09/30/2010
Urea	External Peer-Review Draft Interagency Science Consultation Draft External Peer-Review Meeting	09/28/2010 09/28/2010 12/13/2010
Formaldehyde-Inhalation Assessment	External Peer-Review Draft Interagency Science Consultation Draft Listening Session	06/02/2010 06/02/2010 07/27/2010
Dioxin Reanalysis	External Peer-Review Draft Interagency Science Consultation Draft Listening Session	05/21/2010 05/21/2010 07/09/2010
Hexachloroethane	External Peer-Review Draft Interagency Science	05/13/2010 05/13/2010 06/16/2010

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Ask Peter

I'm Peter, the IRIS Virtual Representative. I am an automated response system available weekdays 9 - 5 EST.

I can answer questions from the public about the IRIS Assessments from an extensive database of chemical risk information. Ask Peter

Recently Released Final Reports

- 9/30: **Chloroprene**
- 9/30: **Cis-1,2-dichloroethylene**
- 9/30: **Pentachlorophenol**
- 9/30: **1,1,2,2-Tetrachloroethane**
- 9/30: **Trans-1,2-dichloroethylene**
- 9/28: **Hydrogen Cyanide and Cyanide Salts**
- 8/11: **1,4-Dioxane**

Most Requested IRIS Summaries

- Benzene
- Formaldehyde
- Bisphenol A
- Arsenic, inorganic
- Methylmercury (MeHg)
- Mercury, elemental

IRIS Agenda

- IRIS Nomination Form 2011
- IRIS Agenda and Literature Searches

IRISTrack

Detailed Status Report

	Consultation Draft Listening Session	
Dichloromethane (Methylene Chloride)	External Peer-Review Draft Interagency Science Consultation Draft Listening Session	03/31/2010 03/31/2010 05/11/2010
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For additional assistance or questions about IRIS, contact the IRIS Hotline at (202) 566-1676 (phone), (202) 566-1749 (FAX) or hotline.iris@epa.gov (email).

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An Overview of the IRIS Web site

Welcome to the IRIS Web site & Database! This overview provides you with some information to help you navigate IRIS and understand the subject matter. This website conveys information on assessments posted to the database by the EPA's IRIS Program as well as assessments under development.

For substances with assessments posted to the database, the IRIS website presents health effects information using three different formats:

- Quick View
- IRIS Summary
- Toxicological Review

For assessments under development, the IRIS website provides a tracking tool to help you monitor the status of upcoming substance assessments:

- IRIS Track

The A to Z List of IRIS Substances provides links to each of these health assessment formats and IRIS Track.

Quick View

The IRIS QuickView presents a snapshot of the information available in the IRIS Summary and is intended to be a quick reference guide to key carcinogenic and noncarcinogenic data for each substance contained in the IRIS database. See either the IRIS Summary or the Toxicological Review for a more complete description and greater context.

The format of the QuickView parallels that of the IRIS Summary.

IRIS Summary

The IRIS Summary provides IRIS toxicity values and brief summaries of the information supporting those values, including the critical effect, the principal and supporting studies, uncertainty factors, and key references. The IRIS Summary also includes a revision history and list of synonyms for a given substance.

For more thorough analysis and documentation, a link to the pdf of the Toxicological Review is available on the IRIS Summary page for substances posted to the database since 1997.

Toxicological Review

The Toxicological Review provides scientific support and rationale for the hazard and dose-response risk information in IRIS human health assessments. All Toxicological Reviews are subjected to a full and open independent expert peer review process, including opportunity for public review and comment. Included in the document is information on chemical and physical properties, toxicokinetics, available pharmacokinetic modeling, hazard identification, mode-of-action and dose-response, as well as reference doses (RfD), reference concentrations (RfC), cancer slope factors and unit risks, and cancer descriptors that can be utilized in risk assessments. Toxicological Reviews are available for assessments posted to the IRIS database since 1997.

IRIS Track

The IRIS substance assessment tracking system (IRIS Track) is a compilation of status reports for EPA's IRIS assessments currently in progress. The status report shows the anticipated dates of major milestones, detailing where the substance assessment is in its development.

IRIS Track Milestones:

- **Draft Development:** A health scientist, referred to as a Chemical Manager, is assigned to each substance. The Chemical Manager is responsible for developing the draft assessment and shepherding draft documents though the review process and final ORD/NCEA approval. Development of a draft assessment consists of a literature search and preparation of a draft Toxicological Review (or other background document) and an IRIS Summary. The Chemical Manager may work with a team of toxicologists, epidemiologists, and statisticians in reviewing and analyzing the available literature. EPA's risk assessment guidelines form the basis for the analysis. This work is often supported by an EPA contractor.
- **Agency Review:** The draft assessment is reviewed by a standing group of senior health scientists representing EPA's Offices and Regions and by selected senior health scientists with scientific expertise relevant to the substance under review. The purpose of the IRIS Agency Review is to provide expert internal peer review and Agency-wide consultation to Chemical Managers and to ORD on whether the draft assessment is ready for external peer review and what issues should be raised.
- **Interagency Science Consultation:** EPA sends the draft IRIS Toxicological Review and draft external peer review charge to other Federal agencies and White House offices for a science consultation.
- **External Peer Review and Public Availability:** EPA obtains external peer review, typically via a panel meeting that is open to the public. At this time, the draft assessment is posted on the internet for public comment.
- **Final Assessment:** After a final internal Agency review, a final interagency science discussion, and a determination by EPA that peer review comments have been appropriately addressed, the assessment is uploaded to the IRIS Website.

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IRIS Glossary / Acronyms & Abbreviations

This glossary contains definitions of terms used frequently in IRIS. It is intended to assist users in understanding terms that appear in U.S. EPA hazard and dose-response assessments. These definitions are not all-encompassing, but are useful "working definitions". It is assumed that the user has some familiarity with risk assessment and health science. For terms that are not included in this glossary, the user should refer to standard health science, biostatistics and medical textbooks and dictionaries. [link to IRIS Archive Glossary]

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

A

Acceptable Daily Intake (ADI): The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects.

Acute Exposure: Exposure by the oral, dermal, or inhalation route for 24 hours or less.

Acute Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Acute Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Acute Toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours.

Additional Risk (Added, Attributable Risk or Risk Difference) (AR): The calculated difference in risk of a particular condition between those who are exposed and those who are not. This measure is derived by subtracting the rate (usually incidence or mortality) of the disease among the unexposed persons (Pu) from the corresponding rate among the exposed (Pe), i.e., AR= Pe-Pu. The AR is an absolute measure of the excess risk attributed to exposure.

Adverse Effect: A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge.

Aerodynamic Diameter: The diameter of a sphere with unit density that has aerodynamic behavior identical to that of the particle in question; an expression of aerodynamic behavior of an irregularly shaped particle in terms of the diameter of an idealized particle. Particles having the same aerodynamic diameter may have different dimensions and shapes.

Aerosol: A suspension of liquid or solid particles in air.

Anecdotal Data: Data based on the description of individual cases rather than controlled studies.

Average Daily Dose (ADD): Dose rate averaged over a pathway-specific period of exposure expressed as a daily dose on a per-unit-body-weight basis. The ADD is usually expressed in terms of mg/kg-day or other mass-time units.

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B

Background Levels: Two types of background levels may exist for chemical substances: (a) Naturally occurring levels: Ambient concentrations of substances present in the environment, without human influence; (b) Anthropogenic levels: Concentrations of substances present in the environment due to human-made, non-site sources (e.g., automobiles, industries).

Benchmark Dose (BMD) or Concentration (BMC): A dose or concentration that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background.

BMDL or BMCL: A statistical lower confidence limit on the dose or concentration at the BMD or BMC, respectively.

Benchmark Response (BMR): An adverse effect, used to define a benchmark dose from which an RfD (or RfC) can be developed. The change in response rate over background of the BMR is usually in the range of 5-10%, which is the limit of responses typically observed in well-conducted animal experiments.

Benign Tumor: A tumor that does not spread to a secondary localization, but may impair normal biological function through obstruction or may progress to malignancy later.

Bioassay: An assay for determining the potency (or concentration) of a substance that causes a biological change in experimental animals.

Bioavailability: The degree to which a substance becomes available to the target tissue after administration or exposure.

Biologically Based Dose Response (BBDR) model: A predictive model that describes biological processes at the cellular and molecular level linking the target organ dose to the adverse effect.

Blood-to-air Partition Coefficient: A ratio of a chemical's concentration between blood and air when at equilibrium.

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C

CAS Registry Number: The Chemical Abstract Service Registry Number (CASRN) is an unique numeric identifier, designed to designate only one substance so it can be referenced by many Government Agencies and/or internationally.

Cancer: A disease of heritable, somatic mutations affecting cell growth and differentiation,

characterized by an abnormal, uncontrolled growth of cells.

Carcinogen: An agent capable of inducing cancer.

Carcinogenesis: The origin or production of a benign or malignant tumor. The carcinogenic event modifies the genome and/or other molecular control mechanisms of the target cells, giving rise to a population of altered cells.

Case-control Study: An epidemiologic study contrasting those with the disease of interest (cases) to those without the disease (controls). The groups are then compared with respect to exposure history, to ascertain whether they differ in the proportion exposed to the chemical(s) under investigation.

Chronic Effect: An effect that occurs as a result of repeated or long term (chronic) exposures.

Chronic Exposure: Repeated exposure by the oral, dermal, or inhalation route for more than approximately 10% of the life span in humans (more than approximately 90 days to 2 years in typically used laboratory animal species).

Chronic Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a chronic duration (up to a lifetime) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Chronic Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a chronic duration (up to a lifetime) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Chronic Study: A toxicity study designed to measure the (toxic) effects of chronic exposure to a chemical.

Chronic Toxicity: The capacity of a substance to cause adverse human health effects as a result of chronic exposure.

Co-carcinogen: An agent that, when administered with a carcinogen, enhances the activity of the carcinogen.

Cohort Study (or Prospective Study): An epidemiologic study comparing those with an exposure of interest to those without the exposure. These two cohorts are then followed over time to determine the differences in the rates of disease between the exposure subjects.

Confounder (or Confounding Factor): A condition or variable that is both a risk factor for disease and associated with an exposure of interest. This association between the exposure of interest and the confounder (a true risk factor for disease) may make it falsely appear that the exposure of interest is associated with disease.

Control Group (or Reference Group): A group used as the baseline for comparison in epidemiologic studies or laboratory studies. This group is selected because it either lacks the disease of interest (case-control group) or lacks the exposure of concern (cohort study).

Critical Concentration: An ambient chemical concentration expressed in units of $\mu g/m^3$ and used in the operational derivation of the inhalation RfC. This concentration will be the NOAEL Human Equivalent Concentration (HEC) adjusted from principal study data.

Critical Effect: The first adverse effect, or its known precursor, that occurs to the most sensitive species as the dose rate of an agent increases.

Critical Study: The study that contributes most significantly to the qualitative and quantitative assessment of risk. Also called Principal Study.

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D

Developmental Toxicity: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally until the time of sexual maturation. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth, and functional deficiency.

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. The POTENTIAL DOSE is the amount ingested, inhaled, or applied to the skin. The APPLIED DOSE is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The ABSORBED DOSE is the amount crossing a specific absorption barrier (e.g. the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. INTERNAL DOSE is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by any particular organ or cell is termed the DELIVERED or BIOLOGICALLY EFFECTIVE DOSE for that organ or cell.

Dose-Response Assessment: A determination of the relationship between the magnitude of an administered, applied, or internal dose and a specific biological response. Response can be expressed as measured or observed incidence or change in level of response, percent response in groups of subjects (or populations), or the probability of occurrence or change in level of response within a population.

Dose-Response Relationship: The relationship between a quantified exposure (dose) and the proportion of subjects demonstrating specific biologically significant changes in incidence and/or in degree of change (response).

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E

Effective Dose (ED_{10}): The dose corresponding to a 10% increase in an adverse effect, relative to the control response.

Endpoint: An observable or measurable biological event or chemical concentration (e.g., metabolite concentration in a target tissue) used as an index of an effect of a chemical exposure.

Epidemiology: The study of the distribution and determinants of health-related states or events in specified populations.

Estimated Exposure Dose (EED): The measured or calculated dose to which humans are likely to be exposed considering all sources and routes of exposure.

Excess Lifetime Risk: The additional or extra risk of developing cancer due to exposure to a toxic substance incurred over the lifetime of an individual.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut).

Exposure Assessment: An identification and evaluation of the human population exposed to a toxic agent, describing its composition and size, as well as the type, magnitude, frequency, route and duration of exposure.

Extra Risk (ER): A calculation of risk of adverse effects which adjusts for background incidence rates of the same effects, by estimating risk at dose d only among the fraction of the population not expected to respond to the secondary (background) causes: ER = [P(d)-P(0)/1-P(0)]. For example, if the background rate (P(0)) = 0.8 and the response rate at dose d, P(d)

= .9, then ER = (0.9 - 0.8)/(1-0.8) = 0.1/0.2 = 0.5. That is, at dose d, an additional 10% of the population is expected to respond adversely. But since only 20% of the population was expected to be free of adverse effects without the exposure of interest, this 10% represents 50% of the population that would otherwise have been unharmed by this exposure.

Extrapolation, low dose: An estimate of the response at a point below the range of the experimental data, generally through the use of a mathematical model.

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F

Forced Expiratory Volume (FEV_1): The volume of air that can be forcibly exhaled during the first second of expiration following a maximal inspiration.

Forced Vital Capacity (FVC): The maximal volume of air that can be exhaled as forcibly and rapidly as possible after a maximal inspiration.

Frank Effect Level (FEL): A level of exposure or dose that produces irreversible, adverse effects at a statistically or biologically significant increase in frequency or severity between those exposed and those not exposed.

Functional Residual Capacity (FRC): The lung volume at the end of tidal expiration (TLC - IC).

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G

Gamma (Multi-hit) Model: A generalization of the one-hit model (see definition) for low-dose extrapolation. The probability P(d) that an individual will respond to lifetime, continuous exposure to dose d is given by

$$P(d) = \frac{\lambda^k}{\Gamma(k)} \int_0^d t^{k-1} e^{-\lambda t} dt$$

Where: $\Gamma(k)$ = the gamma function,

k = the number of 'hits' estimated by the model, and

λ = fitted coefficient.

Guidelines (human health risk assessment): Official, peer-reviewed documentation stating current U.S. EPA methodology in assessing risk of harm from environmental pollutants to populations.

Examples:
Guidelines for Carcinogenic Risk Assessment: U.S. EPA guidelines intended to guide Agency evaluation of suspect carcinogens. 66 FR 17765-17817, April 7, 2005.

Guidelines for Exposure Assessment: U.S. EPA guidelines intended to guide Agency analysis of potential exposure to chemical substances. 51 FR 22888-22938, May 29,1992.

Guidelines for Developmental Toxicity Risk Assessment: U.S. EPA guidelines intended to guide Agency analysis of developmental toxicity data. 51 FR 34028-34040, October 1996.

Guidelines for Mutagenicity Risk Assessment: U. S. EPA guidelines intended to guide Agency analysis of mutagenicity data. 51 FR 34006-34016, September,

1986.

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H

Hazard: A potential source of harm.

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans.

Hazard Characterization: A description of the potential adverse health effects attributable to a specific environmental agent, the mechanisms by which agents exert their toxic effects, and the associated dose, route, duration, and timing of exposure.

Human Equivalent Concentration (HEC) or Dose (HED): The human concentration (for inhalation exposure) or dose (for other routes of exposure) of an agent that is believed to induce the same magnitude of toxic effect as the experimental animal species concentration or dose. This adjustment may incorporate toxicokinetic information on the particular agent, if available, or use a default procedure, such as assuming that daily oral doses experienced for a lifetime are proportional to body weight raised to the `0.75 power`.

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I

Incidence: The number of new cases of a disease that develop within a specified population over a specified period of time.

Incidence Rate: The ratio of new cases within a population to the total population at risk given a specified period of time.

Individual Risk: The probability that an individual will experience an adverse effect.

Inhalation Unit Risk: The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/m^3 in air. The interpretation of inhalation unit risk would be as follows: if unit risk = 2 × 10^{-6} per µg/m^3, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical per m^3 of air.

Initiation: The first stage of carcinogenesis.

Interspecies Dose Conversion: The process of extrapolating from animal doses to human equivalent doses.

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L

Latency Period: The time between first exposure to an agent and manifestation or detection of a health effect of interest.

Limited Evidence: A term used in evaluating study data for the classification of a carcinogen by the 1986 U.S. EPA guidelines for carcinogen risk assessment. This classification indicates that a causal interpretation is credible but that alternative explanations such as chance, bias, and confounding variables could not be completely excluded.

Linear Dose Response: A pattern of frequency or severity of biological response that varies directly with the amount of dose of an agent.

Linearized Multistage Procedure: A modification of the multistage model, used for

estimating carcinogenic risk, that incorporates a linear upper bound on extra risk for exposures below the experimental range.

Logistic Model: A dose-response model used for low-dose extrapolation, of the form:

$$P(d) = \gamma + \frac{1-\gamma}{1+e^{-(\alpha+\beta d)}}$$

Where: P(d) = probability of cancer from lifetime, continuous exposure at dose rate d, and

α, β = fitted parameters; and

γ = background incidence rate.

Longer-Term Exposure: Repeated exposure by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10% of the life span in humans (more than 30 days up to approximately 90 days in typically used laboratory animal species).

Lower Limit on Effective Dose$_{10}$ (LED$_{10}$): The 95% lower confidence limit of the dose of a chemical needed to produce an adverse effect in 10 percent of those exposed to the chemical, relative to control.

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Lowest-Observed-Effect Level (LOEL or LEL): In a study, the lowest dose or exposure level at which a statistically or biologically significant effect is observed in the exposed population compared with an appropriate unexposed control group.

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M

Malignant Tumor: An abnormal growth of tissue which can invade adjacent or distant tissues.

Margin of Exposure (MOE): The LED$_{10}$ or other point of departure divided by the actual or projected environmental exposure of interest.

Mass Median Aerodynamic Diameter (MMAD): Median of the distribution of airborne particle mass with respect to the aerodynamic diameter. MMADs are usually accompanied by the geometric standard deviation (g or sigma g) which characterizes the variability of the particle size distribution.

Maximum Likelihood (ML) Method, Maximum Likelihood Estimate (MLE): Statistical method for estimating a population parameter most likely to have produced the sample observations.

Metastasis: The dissemination or secondary growth of a malignant tumor at a site distant from the primary tumor.

Model: A mathematical function with parameters that can be adjusted so the function closely describes a set of empirical data. A mechanistic model usually reflects observed or hypothesized biological or physical mechanisms, and has model parameters with real world interpretation. In contrast, statistical or empirical models selected for particular numerical properties are fitted to data; model parameters may or may not have real world interpretation. When data quality is otherwise equivalent, extrapolation from mechanistic models (e.g., biologically based dose-response models) often carries higher confidence than extrapolation using empirical models (e.g., logistic model).

Modifying Factor (MF): A factor used in the derivation of a reference dose or reference

concentration. The magnitude of the MF reflects the scientific uncertainties of the study and database not explicitly treated with standard uncertainty factors (e.g., the completeness of the overall database). A MF is greater than zero and less than or equal to 10, and the default value for the MF is 1. [Use of a modifying factor was discontinued in 2004.]

Monte Carlo Technique: A repeated random sampling from the distribution of values for each of the parameters in a calculation (e.g., lifetime average daily exposure), to derive a distribution of estimates (of exposures) in the population.

Multistage Model: A mathematical function used to extrapolate the probability of cancer from animal bioassay data, using the form:

$$P(d) = 1 - e^{-(q_0 + q_1 d + q_2 d^2 + \ldots + q_k d^k)}$$

Where: P(d) = probability of cancer from a continuous, lifetime exposure rate d;

q_i = fitted dose coefficients of model; i=0, 1, . . ., k; and

k = number of stages selected through best fit of the model, no greater than one less than the number of available dose groups.

Multistage Weibull Model: A dose-response model for low-dose extrapolation that includes a term for decreased survival time associated with tumor incidence:

$$P(d,t) = 1 - e^{-(q_0 + q_1 d + q_2 d^2 + \ldots + q_k d^k)(t - t_0)^z}$$

Where: P(d,t) = the probability of a tumor (or other response) from lifetime, continuous exposure at dose d until age t (when tumor is fatal);

q_i = fitted dose parameters, i=0, 1, . . ., k;

k = no greater than the number of dose groups - 1;

t_0 = the time between when a potentially fatal tumor becomes observable and when it causes death; and

z = fitted time parameter (also called "Weibull" parameter).

Mutagen: A substance that can induce an alteration in the structure of DNA.

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N

Neoplasm: An abnormal growth of tissue that may be benign or malignant.

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects.

No-Observed-Effect Level (NOEL): An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control.

Non-Linear Dose Response: A pattern of frequency or severity of biological response that does not vary directly with the amount of dose of an agent.

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O

Odds Ratio (OR): A relative measure of the difference in exposure between the diseased (cases) and not diseased (controls) individuals in a case-control study. The OR is interpreted similarly to the relative risk.

Oncogenic: Resulting from a gene that can induce neoplastic transformations in the cell in which it occurs or into which it is introduced.

One Hit Model: A dose-response model based on a mechanistic argument that there is a response after a target site has been hit by a single biologically effective unit of dose within a given time period. The form of the model, a special case of the gamma, multistage, and Weibull models, is given by:

$$P(d) = 1 - e^{(-\lambda d)}$$

Where P(d) = probability of cancer from lifetime continuous exposure at dose rate d, and

λ = fitted dose coefficient.

Oral Slope Factor: An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime oral exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg-day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.

Organoleptic: Affecting or involving a sense organ such as that of taste, smell, or sight.

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P

Physiologically Based Pharmacokinetic (PBPK) Model: A model that 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.

Point of Departure: The dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on dose for an estimated incidence or a change in response level from a dose-response model (BMD), or a NOAEL or LOAEL for an observed incidence, or change in level of response.

ppb: A unit of measure expressed as parts per billion. Equivalent to 1×10^{-9}.

ppm: A unit of measure expressed as parts per million. Equivalent to 1×10^{-6}.

Prevalence: The proportion of disease cases that exist within a population at a specific point in time, relative to the number of individuals within that population at the same point in time.

Probit Model: A dose-response model of the form:

$$P(d) = \gamma + (1 - \gamma)\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\alpha+\beta d} e^{-\frac{u^2}{2}} du$$

Where: P(d) = the probability that an individual selected at random will respond at dose d, assuming a normal distribution of tolerances;

α, β = fitted parameters; and

γ = background response rate.

Promoter: An agent that is not carcinogenic itself, but when administered after an initiator of carcinogenesis, stimulates the clonal expansion of the initiated cell to produce a neoplasm.

Proportionate Mortality Ratio (PMR): The proportion of deaths due to the disease of interest in the exposed population divided by the proportion of deaths due to the disease of interest in the unexposed or reference population. It is frequently converted to a percent by multiplying the ratio by 100.

Prospective Study: See cohort study.

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R

Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments. [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary].

Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments. [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary].

Reference Value (RfV): An estimate of an exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. It is derived from a BMDL, a NOAEL, a LOAEL, or another suitable point of departure, with uncertainty/variability factors applied to reflect limitations of the data used. [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary.] [Reference value is a term proposed in the report, "A Review of the Reference Dose and Reference Concentration Processes" (EPA, 2002), and is a generic term not specific to a given route of exposure. EPA develops numerical toxicity values for the RfD and RfC only; no numerical toxicity values are developed for the RfV.]

Regional Deposited Dose (RDD): The deposited dose of particles calculated for a respiratory tract region of interest (r) as related to an observed toxicity. For respiratory effects of particles, the deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq. cm). For extra respiratory effects of particles, the deposited dose in the total respiratory system is adjusted for ventilatory volumes and body weight (mg/min-kg).

Regional Deposited Dose Ratio (RDDR): The ratio of the regional deposited dose calculated for a given exposure in the animal species of interest to the regional deposited dose of the same exposure in a human. This ratio is used to adjust the exposure effect level for interspecies dosimetric differences to derive a human equivalent concentration for particles.

Regional Gas Dose: The gas dose calculated for the region of interest as related to the observed effect for respiratory effects. The deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq.cm).

Regional Gas Dose Ratio (RGDR): The ratio of the regional gas dose calculated for a given exposure in the animal species of interest to the regional gas dose of the same exposure in humans. This ratio is used to adjust the exposure effect level for interspecies dosimetric differences to derive a human equivalent concentration for gases with respiratory effects.

Relative Risk (or Risk Ratio (RR)): The relative measure of the difference in risk between the exposed and unexposed populations in a cohort study. The relative risk is defined as the rate of disease among the exposed divided by the rate of the disease among the unexposed. A relative risk of 2 means that the exposed group has twice the disease risk as the unexposed group.

Reserve Volume: The volume of air remaining in the lungs after a maximal expiration.

Residual Volume (RV): The lung volume after maximal expiration (TLC - VC).

Risk (in the context of human health): The probability of adverse effects resulting from exposure to an environmental agent or mixture of agents.

Risk Assessment (in the context of human health): The evaluation of scientific information on the hazardous properties of environmental agents (hazard characterization), the dose-response relationship (dose-response assessment), and the extent of human exposure to those agents (exposure assessment). The product of the risk assessment is a statement regarding the probability that populations or individuals so exposed will be harmed and to what degree (risk characterization).

Risk Characterization: The integration of information on hazard, exposure, and dose-response to provide an estimate of the likelihood that any of the identified adverse effects will occur in exposed people.

Risk Management (in the context of human health): A decision making process that accounts for political, social, economic and engineering implications together with risk-related information in order to develop, analyze and compare management options and select the appropriate managerial response to a potential chronic health hazard.

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Short-Term Exposure: Repeated exposure by the oral, dermal, or inhalation route for more than 24 hours, up to 30 days.

Short-term Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for short-term duration (up to 30 days) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Short-term Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a short-term duration (up to 30 days) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Sigma g (s g): Geometric standard deviation. (See Mass Median Aerodynamic Diameter.)

Slope Factor: An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of

proportion (of a population) affected per mg/kg-day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.

Standardized Mortality Ratio (SMR): This is the relative measure of the difference in risk between the exposed and unexposed populations in a cohort study. The SMR is similar to the relative risk in both definition and interpretation. This measure is usually standardized to control for any differences in age, sex, and/or race between the exposed and reference populations. It is frequently converted to a percent by multiplying the ratio by 100.

Statistical Significance: The probability that a result is not likely to be due to chance alone. By convention, a difference between two groups is usually considered statistically significant if chance could explain it only 5% of the time or less. Study design considerations may influence the a priori choice of a different level of statistical significance.

Subchronic Exposure: Repeated exposure by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10% of the life span in humans (more than 30 days up to approximately 90 days in typically used laboratory animal species). [See also longer-term exposure.]

Subchronic Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a subchronic duration (up to 10% of average lifespan) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Subchronic Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a subchronic duration (up to 10% of average lifespan) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Subchronic Study: A toxicity study designed to measure effects from subchronic exposure to a chemical.

Sufficient Evidence: A term used in evaluating study data for the classification of a carcinogen under the 1986 U.S. EPA guidelines for carcinogen risk assessment. This classification indicates that there is a causal relationship between the agent or agents and human cancer.

Superfund: Federal authority, established by the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) in 1980, to respond directly to releases or threatened releases of hazardous substances that may endanger health or welfare.

Supporting Studies: Studies that contain information useful for providing insight and support for conclusions.

Susceptibility: Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic).

Susceptible Subgroups: May refer to life stages, for example, children or the elderly, or to other segments of the population, for example, asthmatics or the immune-compromised, but are likely to be somewhat chemical-specific and may not be consistently defined in all cases.

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point.

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Target Organ: The biological organ(s) most adversely affected by exposure to a chemical, physical, or biological agent.

Teratogenic: Structural developmental defects due to exposure to a chemical agent during formation of individual organs.

Threshold: The dose or exposure below which no deleterious effect is expected to occur.

Tidal Volume (V_T): The volume of air inhaled/exhaled during normal breathing.

Total Lung Volume (TLV): The lung volume at maximal inspiration.

Toxicity: Deleterious or adverse biological effects elicited by a chemical, physical, or biological agent.

Toxicodynamics: The determination and quantification of the sequence of events at the cellular and molecular levels leading to a toxic response to an environmental agent (sometimes referred to as pharmacodynamics).

Toxicokinetics: The determination and quantification of the time course of absorption, distribution, biotransformation, and excretion of chemicals (sometimes referred to as pharmacokinetics).

Toxicology: The study of harmful interactions between chemical, physical, or biological agents and biological systems.

Toxic Substance: A chemical, physical, or biological agent that may cause an adverse effect or effects to biological systems.

Tumor: An abnormal, uncontrolled growth of cells. Synonym: neoplasm

Tumor Progression: Under the Armitage-Doll multistage theory of cancer development, the transition of a cell line between the stages which lead to cancer.

Threshold Limit Value (TLV): Recommended guidelines for occupational exposure to airborne contaminants published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs represent the average concentration in mg/m^3 for an 8-hour workday and a 40-hour work week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

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Uncertainty: Uncertainty occurs because of a lack of knowledge. It is not the same as variability. For example, a risk assessor may be very certain that different people drink different amounts of water but may be uncertain about how much variability there is in water intakes within the population. Uncertainty can often be reduced by collecting more and better data, whereas variability is an inherent property of the population being evaluated. Variability can be better characterized with more data but it cannot be reduced or eliminated. Efforts to clearly distinguish between variability and uncertainty are important for both risk assessment and risk characterization.

Uncertainty/Variability Factor (UFs): One of several, generally 10-fold, default factors used in operationally deriving the RfD and RfC from experimental data. The factors are intended to account for (1) variation in susceptibility among the members of the human population (i.e., inter-individual or intraspecies variability); (2) uncertainty in extrapolating animal data to humans (i.e., interspecies uncertainty); (3) uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure (i.e., extrapolating from subchronic to chronic exposure); (4) uncertainty in extrapolating from a LOAEL rather than from a NOAEL; and (5) uncertainty associated with extrapolation when the database is incomplete.

Unit Risk: The upper-bound excess lifetime cancer risk estimated to result from continuous

exposure to an agent at a concentration of 1 µg/L in water, or 1 µg/m^3 in air. The interpretation of unit risk would be as follows: if unit risk = 2 × 10^{-6} per µg/L, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical per liter of drinking water.

Upper bound: A plausible upper limit to the true value of a quantity. This is usually not a true statistical confidence limit.

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Variability: Variability refers to true heterogeneity or diversity. For example, among a population that drinks water from the same source and with the same contaminant concentration, the risks from consuming the water may vary. This may be due to differences in exposure (i.e., different people drinking different amounts of water and having different body weights, different exposure frequencies, and different exposure durations) as well as differences in response (e.g., genetic differences in resistance to a chemical dose). Those inherent differences are referred to as variability. Differences among individuals in a population are referred to as inter-individual variability, differences for one individual over time is referred to as intra-individual variability.

Vital Capacity (VC): The maximum volume that can be exhaled in a single breath (TLC-RC).

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Weibull Model: A dose-response model of the form:

$$P(d) = \gamma + (1 - \gamma)(1 - e^{-\beta d^{\alpha}})$$

Where: P(d) = the probability of a tumor (or other response) from lifetime, continuous exposure at dose d until age t (when tumor is fatal);

α = fitted dose parameter (sometimes called "Weibull" parameter);

β = fitted dose parameter;

γ = background response rate.

Weight-of-Evidence (WOE) for Carcinogenicity: A system used by the U.S. EPA for characterizing the extent to which the available data support the hypothesis that an agent causes cancer in humans. Under EPA's 1986 risk assessment guidelines, the WOE was described by categories "A through E", Group A for known human carcinogens through Group E for agents with evidence of noncarcinogenicity. The approach outlined in EPA's guidelines for carcinogen risk assessment (2005) considers all scientific information in determining whether and under what conditions an agent may cause cancer in humans, and provides a narrative approach to characterize carcinogenicity rather than categories. Five standard weight-of-evidence descriptors are used as part of the narrative.

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Frequent Questions

What is IRIS?

EPA's Integrated Risk Information System (IRIS) is a human health assessment program that evaluates risk information on effects that may result from exposure to environmental contaminants. Through the IRIS Program, EPA provides the highest quality science-based human health assessments to support the Agency's regulatory activities. The IRIS database contains information for more than 540 chemical substances containing information on human health effects that may result from exposure to various substances in the environment. IRIS is prepared and maintained by the EPA’s National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD).

The heart of the IRIS system is its collection of searchable documents that describe the health effects of individual substances and that contain descriptive and quantitative information in the following categories:

- **Noncancer effects:** Oral reference doses and inhalation reference concentrations (RfDs and RfCs, respectively) for effects known or assumed to be produced through a nonlinear (possibly threshold) mode of action. In most instances, RfDs and RfCs are developed for the noncarcinogenic effects of substances.
- **Cancer effects:** Descriptors that characterize the weight of evidence for human carcinogenicity, oral slope factors, and oral and inhalation unit risks for carcinogenic effects. Where a nonlinear mode of action is established, RfD and RfC values may be used.

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What substances are in IRIS?

A complete alphabetical list of the substances in IRIS is available at the A to Z List of IRIS Substances on the left navigation bar. Use Search the IRIS Database by substance name or CASRN to search for IRIS assessments for a specific substance. Other specific search criteria are available as well. You can also search multiple substances at once using Compare IRIS Values.

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What is an RfD and RfC?

EPA's IRIS is a human health assessment program that evaluates quantitative and qualitative risk information on effects that may result from exposure to specific chemical substances found in the environment. The IRIS database contains information that can be used to support the first two steps (hazard identification and dose-response evaluation) of the risk assessment process. When supported by available data, IRIS provides oral reference doses (RfDs) and inhalation reference concentrations (RfCs) for chronic non-cancer health effects, and oral slope factors and inhalation unit risks for carcinogenic effects. Combined with specific exposure information, government and private entities use IRIS to help characterize public health risks of chemical substances in a site-specific situation and thereby support risk management decisions designed to protect public health.

More specifically, the reference dose (RfD) and reference concentration (RfC) provide quantitative information for use in risk assessments for health effects known or assumed to be produced through a nonlinear (possibly threshold) mode of action. The RfD (expressed in units of mg of substance/kg body weight-day) is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. An RfD can be derived from a no-observed-adverse-effect level (NOAEL), lowest-observed-adverse-effect level (LOAEL), or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. The inhalation RfC (expressed in units of mg of substance/m^3 air) is analogous to the oral RfD but provides a continuous inhalation exposure estimate. The inhalation RfC considers toxic effects for both the respiratory system (portal of entry) and effects peripheral to the respiratory system (extrarespiratory or systemic effects). Reference values may also be derived for acute (≤24 hours), short-term (>24 hours, up to 30 days), and subchronic (>30 days, up to approximately 10% of the life span) exposure durations, all of which are derived based on an assumption of continuous exposure throughout the duration specified. RfDs and RfCs are generally used in noncancer health assessments.

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What is a cancer weight-of-evidence descriptor?

A cancer weight-of-evidence (WOE) descriptor is used by IRIS to describe a substance's potential to cause cancer in humans and the conditions under which the carcinogenic effects may be expressed. This judgment is independent of consideration of the agent's carcinogenic potency. Under EPA's 1986 guidelines for carcinogen risk assessment, the WOE was described by categories "A through E"—Group A for known human carcinogens through Group E for agents with evidence of noncarcinogenicity. Under the EPA's 2005 guidelines for carcinogen risk assessment, a narrative approach, rather than categories, is used to characterize carcinogenicity. Five standard weight-of-evidence descriptors (*Carcinogenic to Humans, Likely to Be Carcinogenic to Humans, Suggestive Evidence of Carcinogenic Potential, Inadequate Information to Assess Carcinogenic Potential, and Not Likely to Be Carcinogenic to Humans*) are used as part of the narrative.

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What is a cancer slope factor and unit risk?

Cancer slope factors and unit risks are used to estimate the risk of cancer associated with exposure to a carcinogenic or potentially carcinogenic substance. A slope factor is an upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime

exposure to an agent by ingestion. This estimate, usually expressed in units of proportion (of a population) affected per mg of substance/kg body weight-day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100. A unit risk is an upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water or 1 µg/m^3 in air. The interpretation of unit risk for a substance in drinking water would be as follows: if unit risk = 2 x 10^{-6} per µg/L, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the substance in 1 liter of drinking water.

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How does EPA decide which substances to add or update?

EPA develops a list of substances for IRIS assessment development on an annual basis. The IRIS program submits queries to EPA Program Offices and Regions and the public for nominations for new assessments or updates of assessments currently on IRIS. Substances are selected based on one or more of the following factors: (1) potential public health impact; (2) EPA statutory, regulatory, or program-specific implementation needs; (3) availability of new scientific information or methodology that might significantly change the current IRIS information; (4) interest to other governmental agencies or the public; and (5) availability of other scientific assessment documents that could serve as a basis for an IRIS assessment. The decision to assess any given chemical substance depends on available Agency resources. Availability of risk assessment guidance, guidelines, and science policy decisions may also have an impact on the timing of EPA's decision to assess a chemical substance.

The list of new or updated assessments is published in the Federal Register (FR) as part of the IRIS annual agenda.

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How do I generate a Multiple Substances Report?

To compare toxicity values for multiple substances, click on Compare IRIS Values on the left navigation bar. This link allows you to generate summary reports of the toxicity values for multiple substances.

I am interested in Inhalation Toxicology values….should I search using the term “air” or “inhalation”?

Either search term is helpful. Older IRIS assessments generally use the term “air”. This terminology has been updated and changed to “inhalation”. We recommend that you search using both terms, perhaps individually.

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What is the process for developing IRIS assessments?

EPA's process for developing IRIS assessments consists of: (1) a Federal Register announcement of EPA's IRIS agenda and call for scientific information from the public on the selected substances, (2) a search of the current scientific literature, a Federal Register announcement that the literature search is available on the IRIS internet site, and a call to submit additional scientific information on the substance, (3) development of a draft Toxicological Review or other assessment document , (4) internal peer consultation, (5) internal Agency Review, (6) Science Consultation with other Federal agencies and White House offices, (7) external peer review and public comment, (8) final internal Agency Review, Interagency Science Discussion and ORD management approval, and (9) posting on the IRIS database.

This process is described more fully via the IRIS Process page.

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How are IRIS toxicity values used?

IRIS provides hazard identification and dose-response assessment information. The information in IRIS can be used in combination with exposure information to characterize the public health risks of a given substance in a given situation. These risk characterizations can form the basis for risk-based decision-making, regulatory activities, and other risk management decisions designed to characterize and protect public health.

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How do I contact the IRIS Hotline?

Contact the IRIS Hotline via the Contact us page or at (202) 566-1676 (phone), (202) 566-1749 (fax), or hotline.iris@epa.gov (email).

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What is the role of IRIS assessments in risk assessment and risk management?

Risk assessment is a process that has been defined as "the characterization of the potential adverse health effects of human exposures to environmental hazards" (NRC, 1983). Estimates of environmental exposure are combined with the known adverse effects of exposure to determine an overall estimate of the potential public health risk.

A complete risk assessment consists of the following four steps:

1. Hazard identification;
2. Dose-response assessment;
3. Exposure assessment; and
4. Risk characterization.

Hazard identification involves the determination of whether exposure to an agent can cause an increased incidence of an adverse health effect, such as cancer or birth defects, and characterization of the nature and strength of the evidence of causation (NRC, 1994).

Dose-response assessment is the characterization of the relationship between exposure or dose and the incidence and severity of the adverse health effect. It includes consideration of factors that influence dose-response relationships such as intensity and patterns of exposure and age and lifestyle variables that could affect susceptibility. It can involve extrapolation of high-dose responses to low-dose responses and from animal responses to human responses (NRC, 1994).

Exposure assessment is the determination of the intensity, frequency, and duration of actual or hypothetical exposure of humans to the agent in question (NRC, 1994).

The risk characterization integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about risk that is complete, informative, and useful for decision makers (U.S. EPA, 2000). The risk characterization also addresses the uncertainty, assumptions, and scientific judgments of the previous three steps.

An IRIS health assessment consists of the hazard identification and dose-response assessment steps. The information in the IRIS assessment is combined with site- or problem-specific exposure assessments to provide the scientific support for EPA risk management decisions.

EPA considers risk assessment information along with social and economic factors, public health impacts, and statutes and regulations, in deciding how best to protect public health and the environment. Examples of risk management actions include deciding how much of a substance a company may discharge into a river; deciding which substances may be stored at a hazardous waste disposal facility; deciding to what extent a hazardous waste site must be cleaned up; setting permit levels for discharge, storage, or transport; establishing levels for air emissions; and determining allowable levels of contamination in drinking water.

References and further reading:
NRC (National Research Council). 1983. Risk Assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC.

NRC. (1994) Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants, Board on Environmental Studies and Toxicology, Commission on Life Sciences. Washington, DC: National Academy Press.

NRC (2009) Science and Decisions: Advancing Risk Assessments. Committee on Improving Risk Analysis Approaches Used by the U.S. EPA, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies. Washington, DC: the National Academies Press.

US EPA. (2000) Science Policy Council Handbook: Risk Characterization. Washington, DC: Office of Research and Development. EPA 100-B-00-002.

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Tools & Databases

Web Site	Description
Tools	
Benchmark Dose Software	EPA software used for benchmark dose modeling analysis. Available as a free download.
SCIRUS EXIT Disclaimer	A science-specific internet search engine.
Chemical Locators and Databases	
CAL EPA's Department of Pesticide Regulation (DPR) Chemical/Product Database Queries page	Permits a search for: a chemical ingredient by name, CAS number, or DPR chemical code, a chemical ingredient using multiple variables, or registrants by DPR chemical code or CAS Number. You can also search for pesticide products using multiple variables, and view a Report on Registered Active Ingredients.
ChemIDPlus	A dictionary of many chemicals, together with their chemical properties and links to other databases and resources.
ChemFinder.com EXIT Disclaimer	Commercial site for finding chemical structures with links to other databases and resources.
National Institute of Occupational Safety and Health -- NIOSH's databases	Numerous NIOSH data resources are available on this Web site.
National Library of Medicine's Medical Subject Headings (MeSH) Browser	NLM's controlled vocabulary thesaurus. Can be used to help you identify related terms for describing critical effects, precursor effects, and tumor types.
National Pesticide Information Retrieval System (NPIRS)	Database developed by Perdue University and USDA to allow quick retrieval of current information on registered pesticides.

EXIT Disclaimer	
PubMed	Provides access to over 11 million citations from MEDLINE and additional life science journals and includes links to many sites providing full text articles and other related resources.
Science Direct EXIT Disclaimer	Access to scientific journals. Click on "browse A to Z journals" to see a complete list.
US EPA Distributed Structure-Searchable Toxicity (DSSTox) Database Network	A project of EPA's Computational Toxicology Program, helping to build a public data foundation for improved structure-activity and predictive toxicology capabilities. The DSSTox website provides a public forum for publishing downloadable, standardized chemical structure files associated with toxicity data.
US EPA EMCI Chemical Reference Index	Listing of chemicals monitored by EPA's major program systems: Air (AFS), Water (PCS), Hazardous Waste (RCRIS), Superfund (CERCLIS), and Toxics Release Inventory (TRI), including a complete listing of all chemical references.
US EPA ENVIROFACTS Master Chemical Integrator (EMCI)	EMCI allows you to obtain the acronyms, chemical identification numbers, and chemical names reported by the Envirofacts databases (AFS, PCS, RCRAInfo, and TRI).
US EPA OPPTS Resources and Databases	Links to a compilation of Office of Prevention, Pesticides and Toxic Substance's pesticide databases and resources.
US EPA Science Inventory	Listing of all EPA's Science and Research including project descriptions and a list of completed products. Powered by the Environmental Information Management System (EIMS).
US EPA Substance Registry System (SRS)	EPA's central system for information about regulated and monitored substances; provides a common basis for identification of chemicals and biological organisms listed in EPA regulations and data systems, as well as substances of interest from other sources.
US EPA TOXNET	(TOXicology Data NETwork) contains a number of searchable Toxicology databases including the Hazardous Substance Databank (HSDB), Integrated Risk Information System (IRIS), Chemical Carcinogen Research Information System (CCRIS), Toxicology Literature search (TOXLINE), data on mutagenicity studies (GENE-TOX) Developmental and Reproductive Toxicity/Environmental Teratology Information Center (DART/ETIC), Toxics Release Inventory (TRI), and ChemIDPlus.
Web of Science EXIT Disclaimer	Provides access to current and retrospective research journals and contains a unique search tool that allows for forward and backward searching through all available literature.