Glossary of IRIS Terms

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This glossary contains definitions of terms used frequently in IRIS. It is intended to assist users in understanding terms utilized by the U.S. EPA in 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.

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: One dose or multiple doses of short duration spanning less than or equal to 24 hours.

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 (P_u) from the corresponding rate among the exposed (P_e), i.e., AR= P_e-P_u. 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.

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 statistical lower confidence limit on the dose that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background.

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 tool used to estimate potential human health risks by describing and quantifying the key steps in the cellular, tissue and organismal responses as a result of chemical exposure.

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

C

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 which occurs as a result of repeated or long term (chronic) exposures.

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

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, 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.

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-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, percent response in groups of subjects (or populations), or as the probability of occurrence within a population.

Dose-Response Relationship: The relationship between a quantified exposure (dose), and the proportion of subjects demonstrating specific, biological changes (response).

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 disease patterns in human 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.

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 which 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).

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:
Proposed Guidelines for Carcinogenic Risk Assessment: U.S.EPA guidelines intended to guide Agency evaluation of suspect carcinogens. EPA/600/P-92/003C, April 1996.

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, October1996.

Guidelines for the Health Risk Assessment of Chemical Mixtures: U.S. EPA guidelines intended to guide Agency analysis of information relating to health effects from exposure to mixtures of chemical substances. 51 FR 34014-34025, September 1986.

Guidelines for Mutagenicity Risk Assessment: U. S. EPA guidelines intended to guide Agency analysis of mutagenicity data. 51 FR 34006-34016, September, 1986.

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.

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.

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.

Initiation: The first stage of carcinogenesis.

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

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 proportionately 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.

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 statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group. Also referred to as lowest-effect level (LEL).

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.

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 model parameters. Generally provides a mean or central tendency estimate, as opposed to a confidence limit on the estimate.

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.

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 which 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 ($t_0 \geq 1$); and

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

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

N

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

No-Observed-Adverse-Effect Level (NOAEL): An highest exposure level at which there are no statistically or 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, nor precursors to 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 proportionately with the amount of dose of an agent. When mode of action information indicates that responses may not follow a linear pattern below the dose range of the observed data, non-linear methods for determining risk at low dose may be justified.

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 which 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.

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

P

Physiologically Based Pharmacokinetic (PBPK) Model: Physiologically based compartmental model used to characterize pharmacokinetic behavior of a chemical. Available data on blood flow rates, and metabolic and other processes which the chemical undergoes within each compartment are used to construct a mass-balance framework for the PBPK model.

Point of Departure: The dose-response point that marks the beginning of a low-dose extrapolation. This point is most often the upper bound on an observed incidence or on an estimated incidence from a dose-response model.

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.

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.

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.

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 injury, disease, or death from exposure to a chemical agent or a mixture of chemicals. In quantitative terms, risk is expressed in values ranging from zero (representing the certainty that harm will not occur) to one (representing the certainty that harm will occur). The following are examples of how risk is expressed within IRIS: E-4 or 10^{-4} = a risk of 1/10,000; E-5 or 10^{-5} = 1/100,000; E-6 or 10^{-6} = 1/1,000,000. Similarly, 1.3 E-3 or 1.3 x 10^{-3} = a risk of 1.3/1,000=1/770; 8 E-3 or 8 x 10^{-3} = a risk of 1/125 and 1.2 E-5 or 1.2 x 10^{-5} = a risk of 1/83,000.

Risk Assessment (in the context of human health): The determination of potential adverse health effects from exposure to chemicals, including both quantitative and qualitative expressions of risk. The process of risk assessment involves four major steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

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.

S

Short-Term Exposure: Multiple or continuous exposure to an agent for a short period of time, usually one week.

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 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 statistical significance level.

Subchronic Exposure: Exposure to a substance spanning approximately 10% of the lifetime of an organism.

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.

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, at which point effects are produced. Not all chemicals that produce systemic effects cause the same degree of toxicity in all organs.

T

Target Organ: The biological organ(s) most adversely effected by exposure to a chemical substance.

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: The degree to which a chemical substance elicits a deleterious or adverse effect upon the biological system of an organism exposed to the substance over a designated time period..

Toxicology: The study of harmful interactions between chemicals and biological systems.

Toxic Substance: A chemical substance or agent which 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.

U

Uncertainty Factor (UF): One of several, generally 10-fold factors, used in operationally deriving the RfD and RfC from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, i.e., interhuman or intraspecies variability; (2) the uncertainty in extrapolating animal data to humans, i.e., interspecies variability; (3) the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure, i.e., extrapolating from subchronic to chronic exposure; (4) the uncertainty in extrapolating from a LOAEL rather than from a NOAEL; and (5) the uncertainty associated with extrapolation from animal data when the data base 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 = 1.5×10^{-6} µg/L, 1.5 excess tumors are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical in 1 liter of drinking water.

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

V

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

W

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 proposed guidelines for carcinogen risk assessment (1996) 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.

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