Term
Absolute Deviation Definition: The response associated with the BMR will be the background estimate plus or minus the BMR.
Additional Risk Definition: The additional proportion of total animals that respond in the presence of the dose, or the probability of response at dose d, P(d), minus the probability of response in the absence of exposure, P(0).
Adverse Effect Definition: A biochemical change, functional impairment, or pathological lesion that either singly or in combination adversely affects the performance of the whole organism or reduces an organism's ability to respond to an additional environmental challenge.
Akaike Information Criteria Definition: A statistical procedure that provides a measure of the goodness-of-fit of a dose-response model to a set of data. AIC = -2 x (LL - p), where LL is the log-likelihood at the maximum likelihood fit, and p is the degrees of freedom of the model (usually, the number of parameters estimated). Acronym: AIC
Analysis of Deviance Tables Definition: In the tables for the Nested Models, the value for "Full Model" is incorrect. Ignore that value and the comparison with the fitted model in the next line. The likelihood reported in the second line of the table, for "Fitted Model" is correct.
Asymptotic Correlation Matrix

Term
Definition: This table provides the user with a matrix of correlation estimates between each of the parameters. If these values seem to be high (in this case, very close to 1), there may have been a problem in the maximization. High correlation does not confirm that the problem of maximization in fact failed.
Asymptotic Test Definition: Statistical tests that approach known properties as sample sizes increase.
Benchmark Concentration Definition: The concentration of a substance inhaled that is associated with a specified low incidence of risk, generally in the range of 1% to 10%, of a health effect; or the concentration associated with a specified measure or change of a biological effect. Acronym: BMC
Benchmark Dose Definition: An exposure due to a dose of a substance associated with a specified low incidence of risk, generally in the range of 1% to 10%, of a health effect; or the dose associated with a specified measure or change of a biological effect. Acronym: BMD
Benchmark Response Definition: The response, generally expressed as in excess of background (see for example, Extra Risk), at which a benchmark dose or concentration is desired (see Benchmark Dose, Benchmark Concentration). Acronym: BMR

Term
Beta-Binomial Distribution Definition: A statistical distribution of clustered values, e.g., measures on offspring in a litter, where the average proportions of an event for clusters are described by a Beta distribution and the proportions of events in a cluster are described by a binomial distribution.
Binomial Distribution Definition: The statistical distribution of the probabilities of observing 0,1,2,- - - ,n events in a sample of n independent trials each with the same individual probability that the event occurs.
Biologically Significant Effect Definition: A response in an organism or other biological system that is considered to have a substantial or noteworthy effect (positive or negative) on the well- being of the biological system. Used to distinguish statistically significant effects or changes, which may or may not be meaningful to the general state of health of the system.
BMCL Definition: A lower one-sided confidence limit on the BMC.
BMDL Definition: A lower one-sided confidence limit on the BMD.
Bootstrap

Term
Definition: A statistical technique based on multiple resampling with replacement of the sample values or resampling of estimated distributions of the sample values that is used to calculate confidence limits or perform statistical tests for complex situations or where the distribution of an estimate or test statistic cannot be assumed.
Cancer Potency Definition: A number that estimates the cancer risk (incidence) for a lifetime exposure to a substance per unit of dose. Dose is generally expressed as mg/kg body wt/day.
Cancer Slope Factor Definition: See Cancer Potency.
Categorical Data Definition: Results obtained where observations or measurements on individuals or samples are stratified according to degree or severity of an effect, e.g., none, mild, moderate, or severe.
Chi-Square Residual Definition: The values printed at the end of the table are the observed minus expected values, divided by the standard deviation. The overall model should be called into question if the Chi-Square Residual value for any individual dose group, particularly a low dose group, is greater than 2 or less than -2.
Chi-Square Test Definition: A statistical test used to examine the deviation of an observed number of events from an expected number of events.

Term
Chronic Exposure Definition: Long-term exposure usually lasting 6 months to a lifetime.
Clustered Data Definition: Measurements collected on some grouping of individuals, e.g., litters in reproductive and developmental studies.
Confidence Interval (One-Sided) Definition: An interval below the estimated upper confidence limit, or interval above the estimated lower confidence limit, that is expected to include the true value of an estimated parameter with a specified confidence (percent of the time).
Confidence Interval (Two-Sided) Definition: An estimated interval from the lower to upper confidence limit of an estimate of a parameter. This interval is expected to include the true value of the parameter with a specified confidence percentage, e.g., 95% of such intervals are expected to include the true values of the estimated parameters.
Confidence Limit Definition: An estimated value below (or above) which the true value of an estimated parameter is expected to lie for a specified percentage of such estimated limits.
Constant Variance Model

Term
Definition: A BMDS model assumption that the variance of a normal distribution of continuous measures is the same for all dose groups.
Constrained Dose-Response Model Definition: Estimates of one or more parameters of the model are restricted to a specified range, e.g., equal to or greater than zero.
Continuous Data Definition: Effects Measured on a continuum, e.g., organ weight or enzyme concentration, as opposed to quantal or categorical data where effects are classified by assignment to a class.
Continuous Endpoint Definition: A measure of effect that is expressed on a continuous scale (e.g., body weight or serum enzyme levels).
Convergence Definition: Estimates of a parameter approach a single value with increasing sample size or increasing number of computer iterations.
Convex Definition: Region of a dose-response relationship that curves upward, i.e., the slope becomes steeper with increasing dose.
Correlated Binomial Distribution Definition: Clustered data where the individual values in a cluster, e.g., a litter, each have the same probability of expressing an

Term
effect.
Covariate Definition: An independent variable other than dose that may influence the outcome of an effect, e.g., age, body weight, or polymorphism.
Coverage Definition: See confidence intervals or confidence limits.
Critical Effect Definition: The first adverse effect, or its known precursor, that occurs as the dose rate increases.
Critical Study Definition: A bioassay performed on the most sensitive species used as the basis of RfD determination.
Cubic Definition: An effect is a function of a measure raised to the third power.
Degree of the Polynomial Model Setting Definition: The number of times dose is factored into the model equation (maximum=21). A value must be entered here before the model will run. Polynomial degree should not exceed the number of dose groups unless the beta coefficients of the model are

Term
restricted.
Degrees of Freedom Definition: For dose-response model fitting, the number of data points minus the number of model parameters estimated from the data.
Delta Method Definition: Variance of a function of random variables approximated from the derivatives of the function with respect to the random variables and the variances of the random variables.
Developmental Toxicity Definition: Adverse effects on the developing organism that may result from exposure prior to conception or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. Major manifestations of developmental toxicity include death of the developing organism; induction of structural abnormalities (teratogenicity); altered growth; and functional deficiency.
Dichotomous Data Definition: Quantal data where an effect for an individual may be classified by one of two possibilities, e.g., dead or alive, with or without a specific type of tumor.
Dispersion Definition: Variation (differences) from a central (mean or median) value.

Term
dmngb Definition: Written by David M. Gay, this code is used for all models that can be reparameterized so that BMD appears explicitly as a parameter.
donlp2 Definition: Written by P. Spelluci, this code solves optimization problems with non-linear constraints. It is used in cases where the model cannot be so reparameterized.
Dose-Response Model Definition: A mathematical relationship (function) that relates (predicts) a measure of an effect to a dose.
Dose-Response Trend Definition: Relationship between incidence or severity of a biological effect and a function of dose. It is simply the slope for a linear dose-response.
EC_x Definition: Effective exposure concentration associated with a biological effect in x% of the individuals. Often used for inhalation exposures based on the airborne concentration.
ED_x

Term
Definition: Effective dose associated with a biological effect in x% of the individuals. Dose may be the external exposure often expressed in mg per day of the substance per kg body weight raised to a power (generally 1, 3/4, or 2/3) or area under the curve (AUC) in blood or target tissue where the substance remains in the body over a period of time.
Endpoint Definition: An observable or measurable biological or chemical event used as an index of the effect of a chemical on a cell, tissue, organ, organism, etc.
Estimate Definition: An empirical value derived from data for a parameter.
Estimate Intralitter Correlations Definition: Provides user with the option to allow the models to attempt to estimate intralitter correlations or assume they are zero. If "Estimate Intralitter Correlations" is selected (Default), all of the Phi values are estimated (set to -9999 in the model input file).
Excess Risk Definition: Proportion of individuals or animals observed or estimated to possess an effect in addition to the spontaneous background risk.
Extra Risk (Dichotomous Model) Definition: [P(d)-P(0)]/[1 - P(0)], where P(d) is the risk at a dose = d and P(0) is the background risk at zero dose.

Term
Extra Risk (Hill Model) Definition: The maximum (or minimum) achievable response is not 1, but is estimated from the model as Pmax (or Pmin).
Extrapolation Definition: An estimate of response or quantity at a point outside the range of the experimental data. Also refers to the estimation of a measured response in a different species or by a different route than that used in the experimental study of interest (i.e., species-to-species, route-to-route, acute-to-chronic, high-to-low).
Fitted Model Definition: The user-specified model.
Full Model Definition: Yij = Mu(i) + e(ij), Var{e(ij)} = Sigma^2. A Full Model fits all the means at the user specified dose levels. This model also implies a constant variance at each dose level. This likelihood may be of interest in order to determine whether or not a constant variance mode adequately describes the data.
Fullest Model Definition: Yij = Mu(i) +e(ij), Var{e(ij)} = Sigma(i)^2. The Fullest Model would describe a data set that has an individually estimated mean at each dose level, as well as a non-constant variance that does not have any functional relationship to the mean.
Gamma Distribution

Term
Definition: A unimodal statistical distribution (relative proportion of responders as a function of some measure) that is restricted to effects greater than or equal to zero that can describe a wide variety of shapes, e.g., flat, peaked, asymmetrical.
Gaussian (Normal) Distribution Definition: A unimodal symmetrical (bell-shaped) distribution where the most prevalent value is the mean (average) and the spread is measured by the standard deviation. Mathematically, the distribution varies from minus infinity with zero probability to plus infinity with zero probability.
Generalized Estimating Equation Definition: A statistical technique used for estimating parameters that requires only specification of the first two moments of the distribution of the estimator as opposed to a complete specification of the distribution. Acronym: GEE
Genotoxic Definition: A broad term that usually refers to a chemical that has the ability to damage DNA or the chromosomes. This can be determined directly by measuring mutations or chromosome Abnormalities or indirectly by measuring DNA repair, sister-chromatid exchange, etc. Mutagenicity is a subset of genotoxicity.
Goodness-of-Fit Definition: A statistic that measures the dispersion of data about a dose-response curve in 44 order to provide a test for rejection of a model due to lack of an adequate fit, e.g., a P-value <0.1.
Hazard Identification

Term
Definition: Detection of an adverse biological effect, or precursor to an adverse effect, as a result of exposure to a substance.
Hill Equation Definition: A dose-response curve, frequently used for enzyme kinetics, that monotonically approaches an asymptote (maximum value) as a function of dose raised to a power.
Hybrid Model Definition: For continuous data establishes abnormal values based on the extremes in controls (unexposed individuals or animals) and estimates the risk of abnormal levels as a function of dose.
Incidence Definition: Proportion or probability of individuals or animals exhibiting an effect that varies from zero to one, sometimes expressed as a percent from 0% to 100%.
Independence Definition: The result in one animal or individual does not influence the result in another animal or individual.
Initialize a Parameter's Starting Value (advanced mode option) Definition: The user can choose to use the default value, specify a value or initialize the value of each parameter. Each parameter is originally initialized to default values defined for the individual models. Initializing a parameter will cause the program to use the value

Term
entered as a starting point to begin optimization procedures. {If the initialize option is checked for any parameter, the user must input either initialization or starting values for all other parameters.}
Intercept Term Definition: The estimated value at zero dose or the dose corresponding to a zero effect.
Least Squares Definition: A statistical procedure that estimates the values of dose-response parameters such that the sum of squares of deviations of data points from their estimated values is minimized, i.e., minimizes the estimated variance.
Lifetime Definition: Covering the life span of an organism (generally considered 70 years for humans).
Likelihood Function Definition: Relative probabilities that various values of population parameters would arise from the sample observations.
Likelihood Ratio Definition: Ratio of the probability that the observed data arise from a set of model parameters relative to the maximum probability that arises from the set of maximum likelihood estimates.
Linear Dose-Response Model

Term
Definition: The amount of change in a response is proportional to the amount of change in some function of dose.
Linearized Multistage Model Definition: Dose-response model based on the multistage model of carcinogenesis that is restricted to a form that is approximately linear at low doses.
Litter Size (required nested dataset input variable) Definition: Number of live pups per litter.
Litter Specific Covariate Definition: This is a covariate such as body weight of dams, number of implants or litter size that is felt to best explain response variability between litters. It is used in the nested models to try to account for that variability.
Local Maximum Definition: Mathematical solution that maximizes a function in a region that may not be the overall global maximum.
Log Transformation Definition: Logarithm of raw data.
Logistic Model Definition: A sigmoid (S-shaped) function that relates the proportion of individuals with a specified characteristic to an independent

Term
variable, e.g., dose.
Lowest Observed Adverse Effect Level Definition: The lowest dose or exposure level of a chemical in a study at which there is a statistically or biologically significant increase in the frequency or severity of an adverse effect in the exposed population as compared with an appropriate, unexposed control group. See also: NOAEL. Acronym: LOAEL
Margin of Exposure Definition: Ratio of a dose that produces a specified effect, e.g., a benchmark dose, to an expected human dose. Acronym: MOE
Maximum Likelihood Estimate Definition: Estimate of a population parameter most likely to have produced the sample observations. Acronym: MLE
Michaelis-Menten Equation Definition: A dose-response curve, frequently used for enzyme kinetics, with maximum slope at zero dose that approaches a maximum asymptote at increasing dose.
Model Definition: A mathematical representation of a natural system intended to mimic the behavior of the real system, allowing description

Term
of empirical data and predictions about untested states of the system.
Moment Estimates Definition: A statistical estimation procedure that equates population moments to sample moments.
Monotonic Dose-Response Definition: A dose-response that never decreases as dose increases. A monotonic function may be flat (constant) up to a threshold dose or may be flat at high doses if a biological limit, e.g., saturation, is attained.
Multinomial Definition: Animals or individuals may be classified by more than two (binomial) categories, e.g., in a reproductive study fetuses may be dead, alive normal, or alive abnormal.
Nested Data Definition: A nested study is a research design in which the response to be measured (such as developmental effects in pups) is hierarchically embedded (i.e., nested) within the levels of another factor (such as a particular dose of chemical given to the mother). In a nested study with a group of animals, for example, a cohort of dams may be dosed with a chemical, after which each dam will produce a litter of pups. Developmental effects in the pups such as malformations or body weight will be observed, and the observations would be considered nested data, with litter nested within dose group. (Observations made in the dams should be considered cohort data.)
Neurotoxicity

Term
Definition: Ability to damage nervous tissue.
No Observed Adverse Effect Level Definition: An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered as adverse or precursors to adverse effects. In an experiment with several NOAELs, the regulatory focus is primarily on the highest one, leading to the common usage of the term NOAEL as the highest exposure without adverse effect. See also: LOAEL. Acronym: NOAEL
Nonlinear Dose-Response Model Definition: Mathematical relationship that cannot be expressed simply as the change in response being proportional to the amount of change of some function of dose.
Objective Function Definition: Choice of function that is optimized for maximum likelihood estimation.
Ordinal Data Definition: Integers designating the rank, order, or counts.
P-Value Definition: In testing a hypothesis, the probability of a type I error (false positive). The probability that the sample (experimental)

Term
results are compatible with a specific hypothesis.
Parameter Definition: A value used to numerically describe a population of values, e.g., the mean and standard deviation; or a value used to describe a dose-response curve, e.g., the intercept and the slope of a linear dose-response.
Pharmacokinetics Definition: Describes how the body affects a specific chemical after administration through the mechanisms of absorption and distribution, as well as the chemical changes of the substance in the body (e.g. by metabolic enzymes such as cytochrome P450 or glucuronosyltransferase enzymes), and the effects and routes of excretion of the metabolites of the drug. Pharmacokinetic properties of chemicals may be affected by elements such as the site of administration and the dose of the chemical. These may affect the absorption rate. Pharmacokinetics is often studied in conjunction with pharmacodynamics, the study of a chemical’s effect on the body.
Point Definition: Means the response associated with the BMR will be the BMR itself. "Extra" (Hill model only) means the response associated with the BMR will be the background estimate plus or minus the product of the BMR times the difference between the background estimate and the model estimate of the maximum/minimum response.
Point of Departure Definition: The point on a dose-response curve established from experimental data, e.g., the benchmark dose, generally corresponding to an estimated low effect level (e.g., 1% to 10% incidence of an effect). Depending on the mode of action and

Term
available data, some form of extrapolation below the POD may be employed for low-dose risk assessment or the POD may be divided by a series of uncertainty factors to arrive at a reference dose. Acronym: POD
Polynomial Definition: A mathematical function of the sum of a constant, linear term, quadratic term, cubic term, etc.
Population Variability Definition: The concept of differences in susceptibility of individuals within a population to toxicants due to variations such as genetic differences in metabolism and response of biological tissue to chemicals.
Probability Definition: The proportion (on a scale of 0 to 1) of cases for which a particular event occurs. Zero indicates the event never occurs and one indicates the event always occurs.
Probability Distribution Definition: A mathematical description of the relative probabilities of all possible outcomes of a measurement.
Probit Function Definition: Assumes that the relative probabilities of effects as a function of dose are described by a Normal distribution. The cumulative probability as a function of dose has a sigmoid shape.

Term
Profile Likelihood Definition: A plot of the likelihood function versus the estimated value of a parameter.
Quadratic Term Definition: A quantity in a mathematical formula that is raised to the second power (squared).
Quantal Data Definition: Dichotomous (binomial) classification where an individual or animal is placed in one of two categories, e.g., dead or alive, with or without a particular type of tumor, normal or abnormal level of a hormone.
Quantal Endpoint Definition: A dichotomous measure of effect; each animal is scored "normal" or "affected" and the measure of effect is the proportion of scored animals that are affected.
Quantile Definition: Percentile (cumulative probability) of a distribution that ranges from zero to the 100th percentile.
Quasi-Likelihood Definition: Likelihood function that is not totally defined and generally based on only an expression including the mean and variance.
Rectangular Hyperbola

Term
Definition: A mathematical function of the form "y squared equals x squared plus c squared", where x and y are variables and c is a constant.
Reference Concentration Definition: 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. Acronym: RfC
Reference Dose Definition: 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 appreciable risk of deleterious effects during a lifetime. Acronym: RfD
Regression Analysis Definition: A statistical process that produces a mathematical function (regression equation) that relates a dependent variable (biological effect) to independent variable, e.g., dose rate, duration of exposure, age.
Relevant Deviation Definition: Means the response associated with the BMR will be the background estimate plus or minus (depending on the Adverse Direction) the product of the background estimate times the BMR entered by the user.
Repeated Measures

Term
Definition: A biological endpoint is measured for the same individual or animal at different times (e.g., body weight at different ages).
Reproductive Toxicity Definition: Harmful effects on fertility, gestation, or offspring caused by exposure of either parent to a substance.
Residual Variance Definition: The variance in experimental measurements remaining after accounting for the variance due to the independent variables, e.g., dose rate, duration of exposure, age. Typically referred to as the inherent unaccountable experimental variation.
Residuals Definition: The numerical differences between observed and estimated effects.
Response Definition: The biological result of an exposure or dose. Biological responses can be quantified in several ways. Some examples of the type of response data that can be used in a BMD dose-response analysis are dichotomous data (quantal data), nested data, continuous data, and categorical data.
Risk Definition: Probability that an animal or individual exhibits a particular adverse effect for a specified exposure, expressed on a probability scale of 0 to 1. May be expressed as the proportion of a population effected and often converted to the percent effected.

Term
Risk Assessment Definition: The scientific activity of evaluating the toxic properties of a chemical and the conditions of human exposure to it both to ascertain the likelihood that exposed humans will be adversely affected and to characterize the nature of the effects they may experience. The assessment may involve the following four steps: 1) Hazard Identification: The determination of whether a particular chemical is or is not causally linked to particular health effect(s); 2) Dose-Response Assessment: The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question; 3) Exposure Assessment: The determination of the extent of human exposure; and 4) Risk Characterization: The description of the nature and often the magnitude of human risk, including attendant uncertainty.
Risk Characterization Definition: The process of combining dose-response information with exposure information in order to estimate risk.
S-Plus Definition: Computer software for performing statistical analyses.
SAS Definition: Computer software for performing statistical analyses.
Second Degree Definition: A mathematical function that contains a quadratic term.
Shape Parameter

Term
Definition: The exponent on dose in a dose-response function that dictates the curvature of the function.
Significance (Statistical Significance) Definition: See P-value.
Standard Deviation Definition: Means the response associated with the BMR will be the background estimate plus or minus the product of the BMR times the standard deviation about the mean for the control data.
Statistically Significant Effect Definition: In statistical analysis of data, a health effect that exhibits differences between a study population and a control group that are unlikely to have arisen by chance alone.
Subchronic Exposure Definition: Exposure to a substance spanning no more than approximately 10 percent of the lifetime of an organism.
Threshold Dose Definition: Dose below which a specified biological effect does not occur, generally for a particular population. Hence, the threshold dose is for the most sensitive individual in a population.
Threshold Toxicant

Term
Definition: A substance showing an apparent level of effect that is a minimally effective dose, above which a response may occur and which dose no response is expected.
Uncertainty Definition: The unknown effects of parameters, variables, or relationships that cannot or have not been verified or estimated by measurement or experimentation.
Uncertainty Factor Definition: The value (often a default value of 10) used as a divisor of a NOAEL, LOAEL, or benchmark dose to calculate a RfC or RfD. Uncertainty factors are applied as needed for extrapolation of results in experimental animals to humans, inter-individual variability including sensitive subgroups, extrapolation from a LOAEL to a NOAEL, extrapolation of results from subchronic exposures to chronic exposures, and database inadequacies. Acronym: UF
Unconstrained Dose-Response Model Definition: No restrictions imposed on the estimates of parameters.
Upper-Tail Probability Definition: Probability that a variable exceeds a specified value.
Variability

Term
Definition: Observable diversity in biological sensitivity or response, and in exposure parameters (such as breathing rates, food consumption, etc.) These differences can be better understood, but generally not reduced by further research.
Variance Definition: Measure of variability, standard deviation squared.
Weibull Definition: Form of a dose-response curve characterized by a relatively shallow slope at low doses that increases sharply as dose increases before leveling off at high doses.
Weighted Least Squares Estimate Definition: Parameter estimate obtained by minimizing the sum of squares of observed and estimated values weighted by a function, frequently the reciprocal of the variance of an observation.