INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

CHEMISTRY AND HUMAN HEALTH DIVISION

# GLOSSARY FOR TOXICOKINETICS OF CHEMICALS

(IUPAC Recommendations 2003)

*Prepared for publication by*

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## Abstract

This glossary contains definitions of 355 terms frequently used in the multidisciplinary field of toxicokinetics. The glossary is compiled primarily for chemists who find themselves currently working in toxicology and requiring a knowledge of the expressions used in toxicokinetics, especially in relation to hazard and risk assessment. Medical terms are included because of their frequent occurrence in the toxicological literature and because chemists would not normally be expected to be familiar with them. There are three annexes, one containing a list of abbreviations used in toxicokinetics, one containing a list of abbreviations of international bodies and legislation that are relevant to toxicology and chemical safety, and one giving sources of interest for further reading.

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## PREFACE

Within the framework of IUPAC Division VII, Chemistry and Human Health, the project to develop a "Glossary for Toxicokinetics of Chemicals" was initiated in 2001 and approved in 2002. Like many IUPAC bodies, the division is concerned to promote world-wide "regulation, standardization, or codification" in relevant areas of chemistry. Over the years, toxicology and toxicokinetics have grown rapidly in importance. Lack of knowledge and confusion in the terminology currently used in the field of toxicokinetics and chemistry constitutes a problem for the development of the subject. Accordingly, the aim of the project was to compile definitions of the current terminology used in toxicokinetics, including, where relevant, information on chemical speciation, analytical methods, analytical equipment, and biological activity of chemicals.

This glossary is compiled primarily for chemists who now find themselves working in toxicology or requiring a knowledge of the subject. Faced with an extensive literature and terms that are not always defined in accessible dictionaries, newcomers to the subject can have great difficulty in obtaining the background knowledge essential for their work. Further, many toxicologists, whose previous experience has been limited to clinical and experimental toxicology, now have to assess possible toxicological effects of chemicals and need to understand terms used in the relevant literature. There are also regulators and managers who have to interpret toxicological information and therefore need ready access to internationally accepted definitions of relevant terms in common use.

In order to satisfy the requirements of the various groups now concerned with toxicokinetics, the terms included in this glossary have come from a wide range of disciplines and reflect current knowledge and usage. The compilers of this glossary have deliberately included terms peripheral to toxicokinetics but of importance to the subject because they believe that some redundancy of content is preferable to the difficulties currently presented to a newcomer to toxicokinetics in having to consult several dictionaries in order to make a start with the subject.

The definitions given in this glossary are believed to reflect current usage. For some of the entries, alternative definitions are given in order to display the significant differences in the use that been recognized between disciplines.

We are grateful to all those who have contributed to this glossary with constructive criticism and who have suggested modifications for its improvement. Their valuable comments have been incorporated and they are listed on the title page. There will still be flaws but we hope that the final version will be sufficiently close to achieving the original objectives to justify the very widespread support that we have received.

## ACKNOWLEDGEMENTS

The Working Party has met at two occasions, once in Stockholm June 2001 and once in Brussels in April 2003. The Working Party exchanged information with the IUPAC

Commission on Clinical Chemistry regarding terms used in pharmacokinetics. We are grateful to IUPAC for making funds available to support the production of this glossary. A number of persons reflecting various international bodies, organisations and scientists in the field were invited to give comments. A few of the persons that were asked could not give comments due to order of conflict or lack of time. For their active contributions we acknowledge

## NOTES FOR THE USER OF THIS GLOSSARY

Throughout the glossary the following abbreviations are used to indicate the relationships between terms:

AN antonym, opposite
BT broader term
NT narrower term
PS partial synonym
RT related term
SN exact synonym

## ALPHABETICAL ENTRIES

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

**absorbed dose** (of a substance) Amount (of a substance) taken up by an organism or into organs or tissues of interest. See **absorption, systemic**
After Duffus, 1993
SN **internal dose**

**absorbed dose** (of radiation) Energy imparted to a unit mass of matter by ionizing radiation divided by the mass of the absorbing volume.
After ISO, 1972

**absolute lethal concentration** (**$LC_{100}$**) Lowest concentration of a substance in an environmental medium which kills 100 % of test organisms or species under defined conditions. This value is dependent on and may be qualified by the number of organisms used in its assessment.
After WHO, 1979

**absorption** (in biology) Penetration of a substance into an organism by various processes, some specialised, some involving expenditure of energy (active transport), some involving a carrier system, and others involving passive movement down an electrochemical gradient: in mammals absorption is usually through the respiratory tract, gastrointestinal tract, or skin.
After Duffus, 1993

**absorption** (in colloid and surface chemistry) Process whereby, when two phases are brought into contact, a substance is transferred from one phase to the other.
Everett, 1972

**absorption** (of radiation) Phenomenon in which radiation transfers some or all of its energy to matter which it traverses.
ISO, 1972

**Absorption, systemic** Uptake to the blood and transport via the blood of a substance to an organ or compartment in the body distant from the site of absorption.

**absorption coefficient** (in biology) Ratio of the absorbed amount (uptake) of a substance to the administered amount (intake). For exposure by way of the respiratory tract, the absorption coefficient is the ratio of the absorbed amount to the amount of the substance (usually particles) deposited (adsorbed) in the lungs.
IRPTC, 1982
RT **absorbed dose**
SN **absorption factor**

**absorption factor** See preferred SN **absorption coefficient**

**acceptable daily intake (ADI)** Estimate of the amount of a substance in food or drinking water, expressed on a body mass basis (usually mg/kg body weight), which can be ingested daily over a lifetime by humans without appreciable health risk. For calculation of the daily intake per person, a standard body mass of 60 kg is used. (ADI is normally used for food additives: Tolerable Daily Intake (TDI) is the equivalent term used for contaminants.)
WHO, 1991
RT **tolerable daily intake**

**accumulation** See **bioaccumulation**

**activation** See NT **bioactivation**

**active metabolite** Metabolite with biological and or toxicological activity.
RT **metabolite**

**acute**
1. Of short duration, in relation to exposure or effect.
In experimental toxicology, acute refers to studies where dosing is either single or limited to one day although the total study duration may extend to two weeks.
2. In clinical medicine, sudden and severe, having a rapid onset.
After Duffus, 1993
AN **chronic**

**acute effect** Effect of finite duration occurring rapidly (usually in the first 24 h or up to 14 d) following a single dose or short exposure to a substance or radiation.
After Duffus, 1993

**acute exposure** Exposure of short duration.
See RT **acute,** BT **exposure**
AN **chronic exposure**

**acute toxicity**
1. Adverse effects of finite duration occurring within a short time (up to 14 d) after administration of a single dose (or exposure to a given concentration) of a test substance or after multiple doses (exposures), usually within 24 h of a starting point (which may be exposure to the toxicant, or loss of reserve capacity, or developmental change etc.).
2. Ability of a substance to cause adverse effects within a short time of dosing or exposure.
After Duffus, 1993
AN **chronic toxicity**

**additive effect** Consequence which follows exposure to two or more physico-chemical agents which act jointly but do not interact: commonly, the total effect is the simple sum of the effects of separate exposure to the agents under the same conditions.
Duffus, 1993
RT **antagonism, potentiation, synergism**

**adsorption** Increase in the concentration of a substance at the interface of a condensed and a liquid or a gaseous layer owing to the operation of surface forces.
After McNaught and Wilkinson (eds.) (1997)
RT **interfacial layer**

**adsorption factor** Ratio of the amount of substance adsorbed at the interface of a condensed and a liquid or gaseous phase to the total amount of the substance available for adsorption.
RT **interfacial layer**

**advection** Process of transport of a substance in air or water solely by mass motion.

**adverse effect** Change in biochemistry, morphology, physiology, growth, development or lifespan of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to other environmental influences.
After WHO, 1978a

**aerodynamic diameter** (of a particle) Diameter of a spherical particle of unit density which has the same settling velocity in air as the particle in question.
After IPCS, 1989

**aerosol** Stable dispersion of solid particles or droplets in a gas, where the particles or droplets do not settle under the influence of gravity.

**aliquot** Known fractional portion of a homogenous material assumed to be taken with negligible sampling error. The term is usually applied to fluids.

IUPAC, 1994

**allometric** Pertaining to a systematic relationship between growth rates of different parts of an organism and its overall growth rate.
RT **allometric growth**

**allometric growth** Regular and systematic pattern of growth such that the mass or size of any organ or part of a body can be expressed in relation to the total mass or size of the entire organism according to the allometric equation: $Y = bx^{\alpha}$ where Y = mass of the organ, x = mass of the organism, $\alpha$ = growth coefficient of the organ, and b = a constant.
Oxford Concise Veterinary Dictionary, 1988

**allometry** (in biology) Measurement of the rate of growth of a part or parts of an organism relative to the growth of the whole organism.

**allometric scaling**
1. Adjustment of data to allow for change in proportion between an organ or organs and other body parts during the growth of an organism.
2. Adjustment of data to allow for differences and make comparisons between species having dissimilar characteristics, for example in size and shape.
After Dorland, 2000

**antagonism** Combined effect of two or more factors which is smaller than the solitary effect of any one of those factors. In bioassays, the term may be used when a specified response is produced by exposure to either of two factors but not by exposure to both together. The mechanism could be competition for the same receptor (receptor antagonism), changed metabolism, or complex formation (chemical antagonism).
RT **synergism**
SN **antagonistic interaction**

**anthropogenic**
1. Caused by or influenced by human activities.
2. Describing a conversion factor used to calculate a dose or concentration affecting a human that has been derived from data obtained with another species, e.g. the rat.

**apoptosis** Active process of programmed cell death requiring metabolic energy, often characterized by fragmentation of DNA, and not eliciting an inflammatory response.
RT **necrosis**

**area under the concentration-time curve** See BT **area under the curve**

**area under the curve (AUC)** Area between a curve and the abscissa, i. e., the area underneath the graph of a function: often, the area under the tissue (plasma) concentration curve of a substance expressed as a function of time.

**attributable risk** Part of a risk that is identified as due to exposure to a defined substance.
After Last, 2001

See **risk**

**autooxidation** Self-catalysed oxidation reaction that occurs spontaneously in an aerobic environment.

**Bateman function** - Equation expressing the concentration of a substance (usually in plasma) based on first order uptake and elimination in a one compartment model, having the form $C = [fDk_a/V(k_a - k_e)]\bullet[\exp(-k_e t) - \exp(-k_a t)]$ where C is the concentration and D the dose of the substance, f the fraction absorbed, and V the volume of distribution. $k_a$ and $k_e$ are the first order rate constants of uptake and elimination, respectively, and t is time.

**benchmark concentration** Statistical lower confidence limit on the concentration that produces a defined response (called the benchmark response or BMR, usually 5% or 10%) for an adverse effect compared to background, defined as 0%.
After IRIS, 1999
**RT benchmark dose, benchmark response**

**benchmark dose** Statistical lower confidence limit on the dose that produces a defined response (called the benchmark response or BMR, usually 5% or 10%) of an adverse effect compared to background, defined as 0%.
After IRIS, 1999
RT **benchmark concentration, benchmark response**

**benchmark guidance value** Biological monitoring guidance value set at the 90th percentile of available biological monitoring results collected from a representative sample of workplaces with good occupational hygiene practices.
Wilson, 1999

**benchmark response** Response (see definition in this glossary), expressed as an excess of background, at which a benchmark dose or concentration is set.
After IRIS, 1999
RT **benchmark concentration, benchmark dose**

**bioaccumulation** Progressive increase in the amount of a substance in an organism or part of an organism which occurs because the rate of intake exceeds the organism's ability to remove the substance from the body.
PS **bioconcentration, biomagnification**

**bioactivation** Metabolic conversion of a xenobiotic to a more toxic derivative.
Duffus, 1993
PS **activation**
BT **biotransformation**

**bioassay** Procedure for estimating the concentration or biological activity of a substance by measuring its effect on a living system.
After Nagel et al. (eds), 1991
BT **assay**

**bioavailability**

1. Extent of absorption of a substance by a living organism.
SN **biological availability, physiological availability**

2. (in pharmacokinetics) A function of the systemic exposure from extravascular exposure (ev) to that following intravenous (iv) exposure as described by the equation:

$$F = AUC_{ev} * D_{iv} \ / \ AUC_{iv} * D_{ev}$$

where F is the bioavailability, $AUC_{ev}$ and $AUC_{iv}$ are the areas under the plasma concentration time curve following extravascular and intravenous administration and $D_{ev}$ and $D_{iv}$ are the administered extravascular and intravenous doses.
After Duffus, 1993

**bioconcentration** Process leading to a higher concentration of a substance in an organism than in environmental media to which it is exposed.
After WHO, 1979
PS **bioaccumulation, biomagnification**.

**bioconcentration factor (BCF)** Measure of the tendency for a substance in water to accumulate in organisms, especially fish. The equilibrium concentration of a substance in fish can be estimated by multiplying its concentration in the surrounding water by its bioconcentration factor in fish. This parameter is an important determinant for human intake of aquatic food by the ingestion route.
After USEPA, 1986

**bioconjugate** See RT **conjugate**

**bioconversion** see SN **biotransformation**

**bioinactivation** Metabolic conversion of a xenobiotic to a less toxic derivative.

**biokinetics** Science of the movements within developing organisms. Especially in toxicokinetics, science of the movements involved in the distribution of substances.
After Dorland, 2000

**biological assessment of exposure** See SN **biological monitoring**

**biological exposure indices (BEI®)** Guidance value recommended by ACGIH® for assessing biological monitoring results.

**biological half-life, biological half-time ($t_{1/2}$)** Time required for the amount of a substance in a biological system to be reduced to one-half by biological processes, when the rate of decrease is approximately exponential.
After McNaught and Wilkinson (eds.) (1997)
BT **half-life, half-time**

**biological monitoring** Continuous or repeated measurement of potentially toxic substances or their metabolites or biochemical effects in tissues, secreta, excreta, expired air or any combination of these in order to evaluate occupational or environmental exposure and health risk by comparison with appropriate reference

values based on knowledge of the probable relationship between ambient exposure and resultant adverse health effects.
Duffus, 1993
BT **environmental monitoring, monitoring**
SN **biological assessment of exposure**

**biomarker** Indicator signalling an event or condition in a biological system or sample and giving a measure of exposure, effect, or susceptibility; such an indicator may be a measurable chemical, biochemical, physiological, behavioural or other alteration within an organism.
Duffus, 1993

**biomarker of effect** Biomarker that, depending upon the magnitude, can be recognized as associated with an established or possible health impairment or disease.
WHO, 1993

**biomarker of exposure** Biomarker that relates exposure to an exogenous substance to the levels of the substance or its metabolite, or of the product of an interaction between the substance and some target molecule or cell that can be measured in a compartment within an organism.
WHO, 1993
RT **biomarker, exposure**

**biomarker of susceptibility** Biomarker of an inherent or acquired ability of an organism to respond to exposure to a specific substance.
WHO, 1993

**biomonitoring** See SN **biological monitoring**

**biotransformation** Chemical conversion of a substance by living organisms or enzyme preparations derived therefrom.
After Nagel et al. (eds), 1991

**blood-brain barrier** Barrier formed by the blood vessels and supporting tissues of the brain that prevents some substances from entering the brain from the blood.

**blood-testis barrier** Membranous barrier separating the blood from the spermatozoa of the seminiferous tubules and consisting of specific junctional complexes between Sertoli cells.
After Dorland, 2000

**blood plasma** See SN **plasma**

**body burden** Total amount of a substance present in an organism at a given time.
After Duffus, 1993

**carcinogen** n., -ic adj. Agent (chemical, physical or biological) which is capable of increasing the incidence of malignant neoplasms.
IARC, 1987

**carrier** Substance in appreciable amount which, when associated with a trace of a specified substance, will carry the trace with it through a chemical or physical process: carriers may combine in action to form a carrier system.
After McNaught and Wilkinson (eds.) 1997

**carrier-linked prodrug, carrier prodrug** Compound that contains a temporary linkage between a given active substance and a transient carrier group, the latter producing improved physicochemical or pharmacokinetic properties and easily removable *in vivo*.
After Wermuth, 1998

**carrier protein**
1. Protein to which a specific ligand or hapten is conjugated
2. Unlabeled protein introduced into an assay at relatively high concentrations which distributes in a fractionation process in the same manner as labeled protein analyte, present in very low concentrations.
3. Protein added to prevent nonspecific interaction of reagents with surfaces, sample components, and each other.
   After Burtis and Geary, 1994
4. Protein found in cell membranes which facilitates transport of a ligand across the membrane
   RT **carrier substance**

**carrier substance** Substance which binds to another substance and transfers it from one site to another.
RT **carrier protein**

**ceiling value** (**CV**) Airborne concentration of a potentially toxic substance which should never be exceeded in a worker's breathing zone.
Duffus, 1993

**cell line** Defined unique population of cells obtained by culture from a primary source through numerous generations.
After Duffus, 1993
RT **transformed cell line**

**chemical conversion** Change from one chemical species to another.
After Duffus, 1993
PS **conversion**

**chemical species** (of an element) Specific form of an element defined as to isotopic composition, electronic or oxidation state, and/or complex or molecular structure.
PAC, 2000
RT **speciation**

**chronic** Long-term, (in relation to exposure or effect).

1. In experimental toxicology, chronic refers to mammalian studies lasting considerably more than 90 days or to studies occupying a large part of the lifetime of an organism.

2. In clinical medicine, long established or long lasting.

AN **acute**

**chronic effect** Consequence which develops slowly and/or has a long-lasting course: may be applied to an effect which develops rapidly and is long lasting
After WHO, 1979
AN **acute effect**
SN **long-term effect**

**chronic exposure** Continued exposures occurring over an extended period of time, or a significant fraction of the test species' or of the group of individuals', or of the population's life-time.
Duffus, 1993
AN **acute exposure**
SN **long-term exposure**

**chronic toxicity**
1. Adverse effects following chronic exposure.
2. Effects which persist over a long period of time whether or not they occur immediately upon exposure or are delayed
Duffus, 1993
AN **acute toxicity**

**chronotoxicology** Study of the influence of biological rhythms on the toxicity of substances.
Duffus, 1993

**clearance**
1. Volume of blood or plasma or mass of an organ effectively cleared of a substance by elimination (metabolism and excretion) in a given time interval: clearance is expressed in units of volume or mass per unit of time. Total clearance for a component is the sum of the clearances of each eliminating organ or tissue for that component.
2. (in pulmonary toxicology) Removal of any inhaled substance which deposits on the lining surface of the lung; lung clearance is expressed in volume or mass of lung cleared per unit time.
3. (in renal toxicology) Quantification of the removal of a substance by the kidneys by the processes of filtration and secretion; clearance is calculated by relating the rate of renal excretion to the plasma concentration.
Duffus, 1993
RT **elimination**

**comparative risk** See SN **relative excess risk.**

**compartment** Conceptualised part of the body (organs, tissues, cells, or fluids) considered as an independent system for purposes of modelling and assessment of distribution and clearance of a substance.
After WHO, 1979

**compartmental analysis** Mathematical process leading to a model of transport of a substance in terms of compartments and rate constants, usually taking the form C =

$Ae^{-\alpha t} + Be^{-\beta t}$… where each exponential term represents one compartment. C is the substance concentration; A, B, … are proportionality constants; and α, β, … are rate constants.
RT **multicompartment model**

**Concentration, amount-of-substance concentration (c = n/V)** Derived kind-of-quantity defined as the amount of substance (n) of a component divided by the volume (V) of the system containing the component. The fundamental unit is mol $m^{-3}$ but practical units are mol $dm^{-3}$ or mol $L^{-1}$, sometimes denoted by M.
After McNaught and Wilkinson (eds.), 1997

**concentration-effect curve** Graph of the relation between exposure concentration and the magnitude of the resultant biological change.
Duffus, 1993
RT **dose-effect curve**
SN **exposure effect curve**

**concentration-effect relationship** Association between exposure concentration and the resultant magnitude of the continuously graded change produced, either in an individual or in a population.
After Duffus, 1993
RT **dose-effect relationship**

**concentration-response curve** Graph of the relation between exposure concentration and the proportion of individuals in a population responding with a defined effect.
After Duffus, 1993
RT **dose-response curve, response**

**concentration-response relationship** Association between exposure concentration and the incidence of a defined effect in an exposed population.
After Duffus, 1993
RT **dose-response relationship, response**

**congener** One of two or more substances related to each other by origin, structure, or function.
After Duffus, 1993

**conjugate**
1. Derivative of a substance formed by its covalent combination with compounds such as acetic acid, glucuronic acid, glutathione, glycine, or sulfuric acid following reaction wih activated derivatives of these compounds.
RT **phase II reaction**
2. Material produced by attaching two or more substances together, for example - conjugates of antibody with fluorochromes, or enzymes.
After Duffus, 1993

**conjugating enzyme** Protein catalyzing the production of a conjugate by a phase II reaction.
RT **phase II reaction**

**convection** Process by which heat is transferred from one part of a fluid to another by movement of the fluid itself.
Dictionary of Chemistry

**convection (as applied to air and water motion)**
Vertical motion of the air or of water induced by the expansion of the air or water heated by the earth's surface or by human activity and its resulting buoyancy.
After McNaught and Wilkinson (eds.) (1997)

**conversion** See NT **chemical conversion, biotransformation**
Duffus, 1993

**count mean diameter** Mean of the diameters of all particles in a population.
WHO, 1989a
RT **mass mean diameter**

**count median diameter** Calculated diameter in a population of particles in a gas or liquid phase above which there are as many particles with larger diameters as there are particles below it with smaller diameters.
WHO, 1989a
RT **mass median diameter**

**critical concentration** (for a cell or an organ) Concentration of a substance at and above which adverse functional changes, reversible or irreversible, occur in a cell or an organ.
After Duffus, 1993

**critical dose** Dose of a substance at and above which adverse functional changes, reversible or irreversible, occur in a cell or an organ.

**critical effect** For deterministic effects, the first adverse effect which appears when the threshold (critical) concentration or dose is reached in the critical organ: adverse effects with no defined threshold concentration are regarded as critical .
After WHO, 1989a

**critical end-point** Toxic effect used by the USEPA as the basis for a reference dose.
Barnes and Dourson, 1988
RT **reference dose**

**critical group** Part of a target population most in need of protection because it is most susceptible to a given toxicant.
WHO, 1979

**critical organ (**in toxicology) Organ which attains the critical concentration of a substance and exhibits the critical effect under specified circumstances of exposure and for a given population.
After Duffus, 1993

**critical organ concentration** (of a substance) Mean concentration of a substance in the critical organ at the time the substance reaches its critical concentration in the most sensitive type of cell in the organ.
Duffus, 1993
RT **critical concentration, critical organ**

**critical period** (of development) Stage of development of an organism that is of particular importance in the life cycle if the normal full development of some anatomical, physiological, metabolic, or psychological structure or function is to be attained.
After Duffus, 1993

**critical study** Investigation yielding the no observed adverse effect level that is used by the USEPA as the basis of the reference dose.
Barnes and Dourson, 1988
RT **reference dose**
SN **pivotal study**

**cumulative effect** Overall change which occurs after repeated doses of a substance or radiation.
After Duffus, 1993

**cumulative incidence** Number or proportion of individuals in a group who experience the onset of a health-related event during a specified time interval; this interval is generally the same for all members of the group, but, as in lifetime incidence, it may vary from person to person without reference to age.
After Last, 2001

**cumulative incidence rate** Proportion of the cumulative incidence to the total population.
After Last, 2001

**cumulative median lethal dose** Estimate of the total administered amount of a substance which is associated with the death of half a population of animals when the substance is administered repeatedly in doses which are generally fractions of the median lethal dose.
After Duffus, 1993
BT **median lethal dose**

**cytochrome** Heme-containing protein involved in electron transfer reactions.
Alberts et al., 2002

**cytochrome P450** Member of a superfamily of heme-containing monooxygenase enzymes involved in xenobiotic metabolism, cholesterol biosynthesis, and steroidogenesis, in eukaryotic organisms found mainly in the endoplasmic reticulum and inner mitochondrial membrane of cells. 'P450' refers to a feature in the carbon monoxide absorption difference spectrum at 450 nm caused by a thiolate ligand in the fifth position.

**deterministic effect, deterministic process** Phenomenon committed to a particular outcome determined by thermodynamic principles.
RT **critical effect, stochastic effect**

**detoxification**
1. Process, or processes, of chemical modification which make a toxic molecule less toxic.
2. Treatment of patients suffering from poisoning in such a way as to promote physiological processes which reduce the probability or severity of harmful effects.
Duffus, 1993

**diffusion** Spontaneous movement of particles in a system, owing to random thermal motion, to reach an equilibrium concentration throughout the system, and requiring no addition of energy to the system.

**diffusion coefficient (D)** Absolute value of the product of the local number concentration of a component and the local average velocity of particles of that component divided by the number concentration gradient in the direction of movement.
PAC, 1996
$D = h \bullet m/(A \bullet \Delta c \bullet t)$ [i.e., mass = D x Area•(Δc)•time/thickness] This coefficient has dimension of $m^2 s^{-1}$.

**diffusion coefficient** (*D)* Proportionality constant *D*, relating the *flux* of *amount* of entities B to their concentration gradient $\boldsymbol{J_n} = -D$ **grad** *c*B.
After McNaught and Wilkinson (eds.), 1997

**dispersion (**in atmospheric and water chemistry**)** Dilution of a pollutant by spreading in the atmosphere or water due to diffusion or turbulent action (eddy diffusion).
After McNaught and Wilkinson (eds.), 1997

**disposition**
1. Natural tendency shown by an individual or group of individuals, including any tendency to acquisition of specific diseases, often due to hereditary factors.
Duffus, 1993
2. Total of the processes of absorption of a chemical into the circulatory systems, distribution throughout the body, biotransformation, and excretion.

**distribution**
1. Dispersal of a substance and its derivatives throughout the natural environment.
2. Dispersal of a substance and its derivatives throughout an organism,
3. Final location(s) of a substance within an organism after dispersal.
After Duffus, 1993

**distribution constant** Ratio of the concentrations of a single chemical species in two phases, usually organic and aqueous or in chromatographic mobile and stationary phases, at equilibrium.
After Lehman et al., IUPAC Glossary 1996

**distribution volume** Theoretical volume of a body compartment throughout which a substance is calculated to be distributed.

**dominant half-life** Half-life of a substance in a specific organ or compartment which is sufficiently large to define approximately the overall clearance rate at a specific time point.

**dosage** Dose expressed as a function of the mass of the organism being dosed and time, for example mg/(kg body weight)/day: May be used as a synonym for dose.
Duffus, 1993
See RT **dose**

**dose** (of a substance) Total amount (of a substance) administered to, taken up, or absorbed by an organism, organ, or tissue.
After Duffus, 1993
NT **cumulative median lethal dose, lethal dose, maximum tolerable dose, maximum tolerated dose, median effective dose**

**dose-effect** Relation between dose and the magnitude of a measured biological change.
RT **dose-effect relationship**

**dose-effect curve** Graph of the relation between dose and the magnitude of the biological change produced measured in appropriate units.
RT **concentration-effect curve, exposure-effect curve**
Duffus, 1993

**dose-effect relationship** Association between dose and the resulting magnitude of a continuously graded change, either in an individual or in a population.
After Duffus, 1993
RT **concentration-effect relationship, dose-effect**

**dose-response curve** Graph of the relation between dose and the proportion of individuals in a population responding with a defined biological effect.
RT **concentration-response curve, response**
Duffus, 1993

**dose-response relationship** Association between dose and the incidence of a defined biological effect in an exposed population usually expressed as percentage.
After Duffus, 1993
RT **concentration-response relationship, response**

**elimination** Expulsion of a substance from an organism or a part thereof, by processes of metabolism, secretion, or excretion.
WHO, 1979
RT **clearance**

**elimination rate** Differential with respect to time of the concentration or amount of a substance in the body, or a part thereof, resulting from elimination.
RT **rate constant, elimination**

**endocytosis** Uptake of material into a cell by invagination of the plasma membrane and its internalization in a membrane-bounded vesicle.
Alberts et al., 2002
RT **phagocytosis, pinocytosis**

**endothelium** Layer of flattened epithelial cells lining the heart, blood and lymphatic vessels.

**enterohepatic circulation** Cyclical process involving intestinal re-absorption of a substance that has been excreted through the bile, followed by transfer back to the liver, making it available for biliary excretion again.
After Duffus, 1993

**environmental monitoring** Continuous or repeated measurement of agents in the environment to evaluate environmental exposure and possible damage by comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and resultant adverse effects.
RT **biological effect monitoring, biological monitoring, reference value**
Duffus, 1993

**enzyme induction** Biological process which results in an increased biosynthesis of an enzyme thereby increasing its apparent activity.
PAC, 1994

**epithelium** Sheet of one or more layers of cells covering the internal and external surfaces of the body and hollow organs.

**equilibrium** State of a system constant in composition, in which the forces acting on it are balanced and the Gibbs energy is a minimum.

**excretion** Discharge or elimination of an absorbed or endogenous substance, or of a waste product, and/or its metabolites, through some tissue of the body and its appearance in urine, faeces, or other products normally leaving the body. Note that excretion does not include the passing of a substance through the intestines without absorption.
After WHO, 1989a
RT **clearance, elimination**

**excretion rate** Amount of substance and/or its metabolites that is excreted per unit time.
Duffus 1993

**exogenous substance** See preferred SN **xenobiotic**

**exponential decay** Decrease in the amount of a substance, x, with time, t, following the form $dx/dt = f(e^{-t})$.

**exposure**

1. Concentration, amount or intensity of a particular physical or chemical agent or environmental agent that reaches the target population, organism, organ, tissue or cell, usually expressed in numerical terms of substance concentration, duration, and frequency (for chemical agents and micro-organisms) or intensity (for physical agents such as radiation).
2. Process by which a substance becomes available for absorption by the target population, organism, organ, tissue or cell, by any route.
Duffus, 1993

**exposure assessment** Process of measuring or estimating concentration (or intensity), duration and frequency of exposures to an agent present in the environment or, if estimating hypothetical exposures, that might arise from the release of a substance, or radionuclide, into the environment.
Duffus, 1993
RT **risk assessment**

**exposure-effect curve** See SN **concentration-effect curve**

**extracellular space** Volume within a tissue, outside cells and excluding vascular and lymphatic space.
RT **extracellular volume**

**extracellular volume** Volume of fluid outside the cells but within the outer surface of an organism.
RT **extracellular space**

**extraction ratio** Ratio of the amount of substance extracted from a source to the total contained within the source.

**first-order process**
1. Chemical reaction where the rate is directly proportional to the concentration of reactant.
Burtis and Geary, 1994
2. Any process changing at a constant fractional rate.

**first-pass effect** Biotransformation and, in some cases, elimination of a substance in the liver after absorption from the intestine and before it reaches the systemic circulation.
After Duffus, 1993

**first pass metabolism** See SN **first-pass effect**

**foreign substance** See preferred SN **xenobiotic**

**fractionation** Process of classification of an analyte or a group of analytes from a sample according to physical (e.g., size, solubility) or chemical (e.g., bonding, reactivity) properties
Templeton et al., 2000

**gavage** Administration of materials directly into the stomach by oesophageal intubation.
Duffus, 1993

**genetic polymorphism** Existence of inter-individual differences in DNA sequences coding for one specific gene giving rise to different physical and/or metabolic traits.

**genomics**
1.Science of using DNA and RNA based technologies to demonstrate alterations in gene expression.
2. (in toxicology) Method providing information on the consequences for gene expression of interactions of the organism with environmental stress, xenobiotics, etc.

**genotype** Genetic constitution of an organism as revealed by genetic or molecular analysis; the complete set of genes possessed by a particular organism, cell, organelle or virus.
After Nagel et al. (eds), 1991

**genotoxic** Capable of causing a heritable change to the structure of DNA thereby producing a mutation.

**glomerulus** Tuft or a cluster, as of a plexus of capillary blood vessels or nerve fibres, e. g. capillaries of the filtration apparatus of the kidney.
After Duffus, 1993

**glomerular filtration** Formation of an ultrafiltrate of the blood occurring in the glomerulus of the kidney.

**glomerular filtration rate** Volume per unit time of ultrafiltrate formed in the kidney tubules from the blood passing through the glomerular capillaries.

**half-life, half-time, ($t_{1/2}$)** Time in which the concentration of a substance will be reduced by half, assuming a first order process.
After Duffus, 1993
RT **biological half-life**

**hazard** Set of inherent properties of a substance, mixture of substances or a process involving substances that, under production, usage or disposal conditions, make it capable of causing adverse effects to organisms or the environment, depending on the degree of exposure; in other words, it is a source of danger.
Duffus, 1993
RT **risk**

**Henderson-Hasselbach equation** Equation for calculating the degree of dissociation of acids and bases at a given pH; $pH = pK_a + \log([A^-]/[HA])$, where HA is a weak acid, $A^-$ is its conjugate base, and $K_a$ is its acid dissociation constant.

**hepatic** Pertaining to the liver.

**Hill plot** Graphical method for analyzing binding of a molecule A to a macromolecule P with n binding sites. A Hill plot of $\log[\theta/(1-\theta)]$ vs $\log[A]$ has a slope of 1 if binding is non-cooperative and >1 for cooperative binding, where $\theta = [A]_{bound}/n[P]_{total}$ is the fraction of sites occupied.

**incidence** Number of occurrences of illness commencing, or of persons falling ill, during a given period in a specific population: usually expressed as a rate, the denominator being the average number of persons in the specified population during a defined period or the estimated number of persons at the mid-point of that period.
WHO, 1989a

**infusion** (in physiology) Therapeutic introduction of a fluid other than blood, as a (usually saline) solution, into a vein.
After Dorland, 2000

**interfacial layer** Inhomogeneous space region intermediate between two bulk phases in contact, and where properties are significantly different from, but related to, the properties of the bulk phases.
After McNaught and Wilkinson (eds.), 1997

**internal dose** See preferred SN **absorbed dose**

**interstitial fluid** Aqueous solution filling the narrow spaces between cells.

**intrinsic activity** Maximal stimulatory response induced by a compound in relation to that of a given reference compound.
After Wermuth, 1998

**intrinsic clearance** Volume of plasma or blood from which a substance is completely removed in a period of time under unstressed conditions.

**intrinsic factor** Specific protein required for the absorption of vitamin $B_{12}$ and secreted by cells in the gastric glands of the stomach.

**kinetics** (in chemistry) Branch of chemistry concerned with measuring and studying rates of chemical reactions.
After Daintith, 2000

**latency** See SN **latent period**

**latent period**
1. Delay between exposure to a harmful substance and the manifestations of a disease or other adverse effects
2. Period from disease initiation to disease detection.
After Duffus, 1993
SN **latency**

**lethal concentration** Concentration of a substance in an environmental medium that causes death following a certain period of exposure. (Note: $LC_n$ refers to the median concentration lethal to n % of a test population.)

After WHO, 1979
RT **effective concentration, lethal dose, median lethal concentration**

**lethal dose** Amount of a substance or physical agent (radiation) that causes death when taken into the body (Note: $LD_n$ refers to the median dose lethal to n % of a test population.)
After Duffus, 1993
RT **lethal concentration, median lethal dose**

**lethal synthesis** Metabolic formation of a highly toxic compound often leading to death of affected cells.
After Duffus, 1993

**linearized multistage model** Sequence of steps in which (a) a multistage model is fitted to tumour incidence data; (b) the maximum linear term consistent with the data is calculated; (c) the low-dose slope of the dose-response function is equated to the coefficient of the maximum linear term; and (d) the resulting slope is then equated to the upper bound of potency.
Duffus, 1993
BT **multistage model**

**local effect** Change occurring at the site of contact between an organism and a toxicant.
Duffus, 1993
RT **systemic effect**

**log normal transformation** Transformation of data with a logarithmic function that results in a normal distribution.

**logit transformation** Mathematical transformation that relates response to a stated dose or concentration of a toxicant to the response in the absence of the toxicant by the formula: Logit = log $[B/(B_0-B)]$ where $B$ is the response to the stated dose or concentration and $B_0$ is the response in the absence of the toxicant.
Duffus, 1993

**long-term effect** See SN **chronic effect**

**long-term exposure** See SN **chronic exposure**

**lowest effective dose (LED)** Lowest dose of a chemical inducing a specified effect in a specified fraction of exposed individuals.

**lowest lethal concentration found** See SN **minimum lethal concentration**

**lowest observed adverse effect level (LOAEL)** Lowest concentration or amount of a substance, found by experiment or observation, which causes an adverse alteration of morphology, functional capacity, growth, development, or life span of a target organism distinguishable from normal (control) organisms of the same species and strain under defined conditions of exposure.
Duffus, 1993

RT **adverse effect, lowest observed effect level, no effect level, no observed adverse effect level**

**lowest observed effect level (LOEL)** Lowest concentration or amount of a substance, found by experiment or observation, that causes any alteration in morphology, functional capacity, growth, development, or life span of target organisms distinguishable from normal (control) organisms of the same species and strain under the same defined conditions of exposure.
Duffus, 1993
RT **adverse effect, lowest observed adverse effect level, no effect level, no observed adverse effect level**

**macrophage** Large (10-20 µm diameter) amoeboid and phagocytic cell found in many tissues, especially in areas of inflammation, derived from blood monocytes and playing an important role in host defence mechanisms.
Duffus, 1993
RT **phagocytosis**

**margin of exposure** (**MOE**) Ratio of the no-observed-adverse-effect level (**NOAEL**) to the theoretical or estimated exposure dose (**EED**) or concentration (**EEC**).
Duffus, 1993
RT **therapeutic index**

**margin of safety (MOS)** See SN **margin of exposure**

**mass mean diameter** Diameter of a spherical particle with a mass equal to the mean mass of all the particles in a population.
Duffus, 1993
RT **count mean diameter, count median diameter, mass median diameter**

**mass median diameter** Diameter of a spherical particle with the median mass of all the particles in a population.
IAEA, 1978
RT **count mean diameter, count median diameter, mass mean diameter**

**maximum tolerable concentration (MTC)** Highest concentration of a substance in an environmental medium that does not cause death of test organisms or species (denoted by $LC_0$).
WHO, 1979

**maximum tolerable dose (MTD)** Highest amount of a substance that, when introduced into the body, does not kill test animals (denoted by $LD_0$).
Duffus, 1993

**maximum tolerated dose (MTD)** High dose used in chronic toxicity testing that is expected on the basis of an adequate subchronic study to produce limited toxicity when administered for the duration of the test period. It should not induce (a) overt toxicity, for example appreciable death of cells or organ dysfunction, or (b) toxic manifestations that are predicted materially to reduce the life span of the animals except as the result of neoplastic development or (c) 10 % or greater retardation of

body weight gain as compared with control animals. In some studies, toxicity that could interfere with a carcinogenic effect is specifically excluded from consideration.
Duffus, 1993

**maximum tolerable exposure level (MTEL)** Maximum amount or concentration of a substance to which an organism can be exposed without leading to an adverse effect after prolonged exposure time.
Duffus, 1993

**maximum velocity ($V_{max}$)** In Michaelis-Menten kinetics, the maximum rate of conversion of a substrate when its concentration is not rate limiting.

**mean residence time (MRT)** Average time a drug molecule remains in the body after rapid iv injection: like clearance, its value is independent of dose. After an i.v. bolus:
MRT = AUMC / AUC
AUMC is the area under the first moment of the plasma concentration-time curve: for a drug with one-compartment distribution characteristics, MRT equals the reciprocal of the elimination rate constant.
Beers and Berkow, 1999

**median effective concentration (EC)** Statistically derived concentration of a substance in an environmental medium expected to produce a certain effect in test organisms in a given population under a defined set of conditions. (Note: $EC_n$ refers to the median concentration that is effective in n % of the test population.)
Duffus, 1993
RT **effective concentration**

**median effective dose (ED)** Statistically derived dose of a chemical or physical agent (radiation) expected to produce a certain effect in test organisms in a given population or to produce a half-maximal effect in a biological system under a defined set of conditions. (Note: $ED_n$ refers to the median dose that is effective in n % of the test population.)
Duffus, 1993
**RT effective dose**

**median lethal concentration** ($LC_{50}$) Statistically derived concentration of a substance in an environmental medium expected to kill 50 % of organisms in a given population under a defined set of conditions.
Duffus, 1993

**median lethal dose** ($LD_{50}$) Statistically derived dose of a chemical or physical agent (radiation) expected to kill 50 % of organisms in a given population under a defined set of conditions.
Duffus, 1993

**median lethal time** ($TL_{50}$) Statistically derived average time interval during which 50 % of a given population may be expected to die following acute administration of a chemical or physical agent (radiation) at a given concentration under a defined set of conditions.

Duffus, 1993

**metabolic activation** Biotransformation of a substance to a more biologically active derivative.
BT **activation, biotransformation**
TN **lethal synthesis**
SN **bioactivation**

**metabolic enzymes** Proteins that catalyse chemical transformations of body constituents and, in more common usage, of xenobiotics.
RT **phase I enzymes, phase II enzymes**

**metabolic half-life, metabolic half-time** Time required for one half of the quantity of a substance in the body to be metabolised
After Duffus, 1993
RT **clearance, elimination**

**metabolic model** Analysis and theoretical reconstruction of the way in which the body deals with a specific substance, showing the proportion of the intake that is absorbed, the proportion that is stored and in what tissues, the rate of breakdown in the body and the subsequent fate of the metabolic products, and the rate at which it is eliminated by different organs as unchanged substance or metabolites.
WHO, 1989a

**metabolic transformation** Biotransformation of a substance that takes place within a living organism.
After Duffus, 1993
BT **biotransformation**

**metabolism** Sum total of all physical and chemical processes that take place within an organism; in a narrower sense, the physical and chemical changes that take place in a substance within an organism. It includes the uptake and distribution within the body of a substance, the changes (biotransformation) undergone by such substances, and the elimination of the substance and of their metabolites.
WHO, 1989a
RT **biotransformation, metabolic transformation**

**metabolite** Product resulting from biotransformation.
After WHO, 1979

**metabonomics** Evaluation of tissues and biological fluids for changes in metabolite levels that follow exposure to a given substance, in order to determine the metabolic processes involved and to evaluate the disruption in intermediary metabolic processes that results from exposure to that substance.

**Michaelis constant ($K_m$)** Equilibrium constant in the Michaelis-Menten equation representing the substrate concentration that gives one half the maximal velocity of a catalysed (usually enzymatic) reaction. See Michaelis-Menten kinetics.

**Michaelis-Menten kinetics** Conversion of a substrate (S) to a product (P) in the presence of a catalyst (E) with rate constants *k*, by a mechanism $E + S \leftrightarrow (k_1/k_{-1})$ ES $\leftrightarrow (k_2/k_{-2})$ E + P, thus obeying the so-called Michaelis-Menten equation, $v = V_{max}[S]/(K_m + [S])$, where *v* is the rate of conversion of substrate, $V_{max}$ is the maximum velocity, and $K_m$ is the Michaelis constant.

**midstream sampling** Taking an aliquot of a flowing liquid, such as urine, avoiding initial and terminal flow periods which are likely to be unrepresentative.

**minimum lethal concentration ($LC_{min}$)** Lowest concentration of a toxic substance in an environmental medium that kills individual organisms or test species under a defined set of conditions.
WHO, 1979
SN **Lowest lethal concentration found**

**modifying factor (MF)** see **uncertainty factor**

**monitoring** Continuous or repeated observation, measurement, and evaluation of health and/or environmental or technical data for defined purposes, according to prearranged schedules in space and time, using comparable methods for sensing and data collection. Evaluation requires comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and adverse effects.
After Berlin, Yodaiken, and Henman, 1984; WHO, 1980; Zielhuis and Henderson, 1986
NT **biological monitoring, environmental monitoring**

**Monte Carlo study** Simulation and analysis of a sequence of events using random numbers to generate possible outcomes in an iterative process.

**mucociliary transport** Process of removal of particles from the bronchi of the lungs in a mucus stream moved by cilia, thus contributing to uptake from the gastrointestinal tract.

**Mulliken population analysis** Partitioning scheme based on the use of density and overlap matrices, at one time used for allocating the electrons of a molecular entity in some fractional manner among its various parts (atoms, bonds, orbitals).

**multicompartment model** Product of a compartmental analysis requiring more than two compartments.
RT **compartmental analysis**

**multipotent** Of a cell, capable of giving rise to several different kinds of structure or types of cell.

**multistage model** Dose-response model for cancer death estimation of the form $P(d) = 1 - \exp[-(q_o + q_1d_1 + q_2d_2 + \ldots q_kd_k)]$, where P(d) is the probability of cancer death from a continuous dose rate, d, the q's are constants, and k is the number of dose groups (or, if less than the number of dose groups, k is the number of biological stages

believed to be required in the carcinogenesis process). With the multistage model, it is assumed that cancer is initiated by cell mutations in a finite series of steps.
Duffus, 1993

**multivariate statistics** Set of statistical tools to analyze data matrices using regression and/or pattern recognition techniques.
NT **regression analysis**

**mutagen** Agent that can induce heritable changes (mutations) of the genotype in a cell as a consequence of alterations or loss of genetic material
After Duffus, 1993

**necrosis** Sum of morphological changes resulting from cell death by lysis and/or enzymatic degradation, usually affecting groups of cells in a tissue.

**negligible risk**
1. Probability of adverse effects occurring that can reasonably be described as trivial.
2. Probability of adverse effects occurring that is so low that it cannot be reduced appreciably by increased regulation or investment of resources.
Duffus, 1993

**no effect level (NEL)** Maximum dose (of a substance) that produces no detectable changes under defined conditions of exposure. At present, this term tends to be substituted by no-observed-adverse-effect-level (NOAEL) or no-observed-effect-level (NOEL).
Duffus, 1993
RT **adverse effect, no observed adverse effect level (NOAEL), no observed effect level (NOEL)**

**no observed adverse effect level (NOAEL)** Greatest concentration or amount of a substance, found by experiment or observation, which causes no detectable adverse alteration of morphology, functional capacity, growth, development, or life span of the target organism under defined conditions of exposure.
WHO, 1979.
RT **adverse effect, no effect level (NEL), no observed effect level (NOEL).**
See **uncertainty factor**

**no observed effect level (NOEL)** Greatest concentration or amount of a substance, found by experiment or observation, that causes no alterations of morphology, functional capacity, growth, development, or life span of target organisms distinguishable from those observed in normal (control) organisms of the same species and strain under the same defined conditions of exposure.
Duffus, 1993
RT **adverse effect, no effect level (NEL), no observed adverse effect level (NOAEL)**

**one-compartment model** Kinetic model, where the whole body is thought of as a single compartment in which the substance distributes rapidly, achieving an equlibrium between blood and tissue immediately.
WHO, 1986

**one-hit model** Dose-response model of the form $P(d) = 1 - e^{-bd}$, where P(d) is the probability of cancer death from a continuous dose rate (d) and b is a constant.
After Duffus, 1993

**particulate matter ($PM_n$)** Particles in air, usually of a defined size and specified as $PM_n$ where n is the maximum aerodynamic diameter in µm of at least 50% of the particles.
After WHO, 1999

**partition coefficient** Ratio of the distribution of a substance between two phases when the heterogeneous system of two phases is in equlibrium. The ratio of concentrations (or, strictly speaking, activities) of the same molecular species in the two phases is constant at constant temperature. The octanol/water partition coefficient is often used as a measure of the bioconcentration factor for modelling purposes.
After Duffus, 1993
RT **bioconcentration factor**

**partitioning ratio** Ratio of the concentration of a substance between two compartments in an organism.

**perfusion**
1. (in physiology) Act of pouring over or through, especially the passage of a fluid through the vessels of a specific organ.
2. Liquid poured over or through an organ or tissue.
Dorland, 2000

**phagocytosis** Process by which particulate material is endocytosed by a cell.
Alberts et al., 2002
See **endocytosis.**

**pharmacodynamics** Process of interaction of pharmacologically active substances with target sites, and the biochemical and physiological consequences leading to therapeutic or adverse effects.
Duffus, 1993
RT **adverse effect, target, toxicodynamics.**

**pharmacogenetics** Study of the influence of genetic polymorphisms on the effects of drugs on individual organisms.
After Duffus, 1993
PS **toxicogenetics.**

**pharmacokinetics**
1. Process of the uptake of drugs by the body, the biotransformations they undergo, the distribution of the drugs and their metabolites in the tissues, and the elimination of the drugs and their metabolites from the body over a period of time.
Duffus, 1993
2. The study of such processes.
PS **toxicokinetics.**

RT **biotransformation.**

**pharmacology** Science of the use and effects of drugs: may be subdivided into pharmacokinetics and pharmacodynamics defined above.

**phase I reaction** (of biotransformation) Enzymic modification of a substance by oxidation, reduction, hydrolysis, hydration, dehydrochlorination or other reactions catalysed by enzymes of the cytosol, of the endoplasmic reticulum (microsomal enzymes) or of other cell organelles.
Duffus, 1993
BT **biotransformation**
RT **cytochrome P-450 family, phase II reaction, phase III reaction**

**phase II reaction** (of biotransformation) Binding of a substance, or its metabolites from a phase 1 reaction, with endogenous molecules (conjugation), making more water-soluble derivatives that may be excreted in the urine or bile.
Duffus, 1993
BT **biotransformation**
RT **conjugate, phase I reaction, phase III reaction**

**phase III reaction** (of biotransformation) Further metabolism of conjugated metabolites produced by phase II reactions.
After Duffus, 1993
BT **biotransformation**
RT **conjugate, phase I reaction, phase II reaction**

**phenotype** The observable structural and functional characteristics of an organism determined by its genotype and modulated by its environment.
Nagel et al. (eds), 1991
RT **genotype**

**physiological pharmacokinetic model** See **physiologically based pharmacokinetic modelling.**

**physiologically based pharmacokinetic modelling (PBPK)** Mathematical modelling of kinetic behaviour of a substance, based on measured physiological parameters.
SN **toxicologically based pharmacokinetic modelling (TBPK)**

**pinocytosis** Type of endocytosis in which soluble materials are taken up by the cell and incorporated into vesicles for digestion.
After Alberts et al., 2002

**pivotal study** See SN **critical study**

**plasma** (in biology)
1. Fluid component of blood in which the blood cells and platelets are suspended.
   SN **blood plasma.**
2. Fluid component of semen produced by the accessory glands, the seminal vesicles, the prostate, and the bulbo-urethral glands.

3. Cell substance outside the nucleus (Obsolete). SN **cytoplasm**
Duffus, 1993

**poison** Substance that, taken into or formed within the organism, impairs the health of the organism and may kill it.
After Duffus, 1993
SN **toxicant, toxic substance.**

**population at risk** Persons who can and may develop an adverse health effect and who are potentially exposed to a substance under study. People already having chronic disease are excluded from the population at risk in studies of the incidence of the adverse effect.
After WHO, 1979

**potency** (in toxicology) Expression of relative toxicity of an agent as compared to a given or implied standard or reference.
After Duffus, 1993

**potentiation** (in toxicology) Enhancement by an agent, at a concentration that has a different or no (effect), of the harm done by another agent.
RT **additive effect, antagonism, synergism**

**procarcinogen** Substance that has to be metabolized before it becomes a carcinogen.
After Duffus, 1993

**prodrug** Inactive precursor converted to an active form of a drug within the body**.**

**proteome** Complete set of proteins encoded by the genome.

**proteomics** Global analysis of gene expression using a variety of techniques to identify and characterize proteins. It can be used to study changes caused by exposure to chemicals and to determine if changes in mRNA expression correlate with changes in protein expression: the analysis may also show changes in post-translational modification, which cannot be distinguished by mRNA analysis alone.

**pulmonary** Pertaining to the lungs.

**quantal** Describing a condition that can be expressed only as occurring or not occurring, such as death.
After Duffus, 1993
AN **graded effect**
RT **stochastic effect**
SN **all-or-nothing effect**

**quantitative structure-activity relationship (QSAR)** Quantitative association between the physicochemical and/or structural properties of a substance and its biological properties, including its toxicity.
After Duffus, 1993

**quantitative structure metabolism relationship (QSMR)** Quantitative association between the physicochemical and/or the structural properties of a substance and its metabolic behavior.

**rate constant** Proportionality that relates the speed of a chemical reaction to some function of reactant concentrations
After Morris, 1992

**rate-limiting step** Single step in a multistep reaction, the rate constant for which exerts a dominant effect on the overall rate.

**reactive oxygen species (ROS)** Intermediates in the reduction of molecular $O_2$ to water, i.e. superoxide anion $O_2^{-\bullet}$, hydrogen peroxide $H_2O_2$, and hydroxyl radical HO•.

**receptor** Molecular structure in or on a cell that specifically recognizes and binds a compound acting as a physiological signal transducer or mediator of an effect.

**receptor-mediated endocytosis** Endocytosis of a substance and its receptor following receptor binding.

**reconstitution** Restoration to original form of a substance previously altered for preservation and storage.
After Dorland, 2000

**reference dose (RfD)** Term used for 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 appreciable risk of deleterious effects during a lifetime.
Barnes and Dourson, 1988
RT **acceptable daily intake**
BT **dose**
See RT **uncertainty factor**

**regioselective** Describing a chemical reaction in which one direction of bond making or breaking occurs preferentially over all others.

**regression analysis** Statistical methods for modeling a set of dependent variables, Y, in terms of combinations of predictors, X.

**relative excess risk (RER)** Measure that can used in comparison of adverse reactions to drugs, other exposures, based solely on the component of risk due to the exposure or drug under investigation, removing the risk due to background exposure experienced by all in the population. $RER = (R_1-R_0) / (R_2-R_0)$ where $R_1$ is the rate in the population, $R_2$ is the rate in the comparison population, and $R_0$ is the rate in the general population.
After Last 2001

**relative risk**
1. Ratio of the risk of disease or death among the exposed to the risk among the unexposed; the risk ratio.

2. Ratio of the cumulative incidence rate in the exposed to the cumulative incidence rate in the unexposed; the rate ratio.
After Last, 2001

**relative systemic availability** Ratio of metabolizable substance to absorbed substance per unit exposure.

**renal** Pertaining to the kidneys.

**renal plasma flow** Volume of plasma passing through the kidneys in unit time.

**reservoir** Storage compartment from which a substance may be released with subsequent biological effects.

**residence time** See **mean residence time (MRT)**

**residual risk** Health risk remaining after risk reduction actions are implemented.

**residual time** See RT **mean residence time (MRT)**

**respirable dust, respirable particles** Mass fraction of dust (particles) that penetrates to the unciliated airways of the lung (the alveolar region): it is represented by a cumulative log-normal curve having a median aerodynamic diameter of 4.25 µm and a standard deviation of 1.5 (values for humans).
ACGIH® 1985
**RT particulate matter ($PM_n$)**

**response** Proportion of an exposed population with a defined effect or the proportion of a group of individuals that demonstrates a defined effect in a given time at a given dose rate.
After Duffus, 1993
RT **dose-response relationship**

**retention**
1. Amount of a substance that is left from the total absorbed after a certain time following exposure.
2. Holding back within the body or within an organ, tissue or cell of matter that is normally eliminated.
After Duffus, 1993
AN **elimination**

**risk**
1. Probability of adverse effects caused under specified circumstances by an agent in an organism, a population or an ecological system.

IOMC, 1999

2. Expected frequency of occurrence of a harmful event arising from such an exposure.
After Duffus, 1993

**risk assessment** Identification and quantification of the risk resulting from a specific use or occurrence of an agent, taking into account possible harmful effects on individuals exposed to the agent in the amount and manner proposed and all the possible routes of exposure. Quantification ideally requires the establishment of dose-effect and dose-response relationships in likely target individuals and populations.
Duffus, 1993
RT **exposure assessment, hazard identification, risk characterization, risk estimation, risk evaluation, risk identification, risk management, risk perception**

**safety factor(SF)** see RT **uncertainty factor**

**sample** (in statistics)
1. Group of individuals often taken at random from a population for research purposes.
2. One or more items taken from a population or a process and intended to provide information on the population or process.
Duffus, 1993
3. Portion of material selected from a larger quantity so as to be representative of the whole.
Horwitz, 1990, Duffus, 1993

**sampling** Act of obtaining a sample (see aliquot).
After Duffus, 1993
RT **sample, sampling error**

**sampling error** Part of the total estimation error of a parameter (or value of a property, such as concentration) caused by intrinsic variability of sampling and by the random nature of the sample.
After Duffus, 1993
RT **sample, sampling**

**saturable elimination** Elimination that becomes concentration-independent at a concentration at which the elimination process is functioning maximally.

**Scatchard plot** - Method for analysing data for freely reversible ligand/receptor binding interactions. The graphical plot is (Bound ligand/Free ligand) against (Bound ligand). The slope gives the negative reciprocal of the binding affinity and the intercept on the x axis the number of receptors.
RT **Hill plot**

**second messenger** Intracellular effector substance increasing or decreasing as a response to the stimulation of a receptor by an agonist, considered as the "first messenger".
After Wermuth, 1998

**serum**
1. Watery proteinaceous portion of the blood that remains after clotting.
SN **blood serum**.
2. Clear watery fluid especially that moistening the surface of serous membranes or that exuded through inflammation of any of these membranes.

Duffus, 1993

**short term exposure limit (STEL)** Fifteen minute time weighted average exposure recommended by ACGIH® which should not be exceeded at any time during a workday, even if the 8-hour TWA is within the TLV®-TWA.
ACGIH®, 2002
RT **threshold limit value® (TLV®), time weighted average (TWA).**

**speciation** (in chemistry) Distribution of an element amongst defined chemical species in a system.
Templeton et al., 2000
RT **speciation analysis**

**speciation analysis** (in chemistry) Analytical activities of identifying and/or measuring the quantities of one or more individual chemical species in a sample
Templeton et al., 2000
RT **speciation**

**steady state** State of a system in which the conditions do not change in time
Morris, 1992

**stem cell** Multipotent cell with mitotic potential that may serve as a precursor for many kinds of differentiated cells.

**stereoselective synthesis** Chemical reaction (or reaction sequence) in which one or more new elements of chirality are formed in a substrate molecule and which produces the stereoisomeric (enantiomeric or diastereoisomeric) products in unequal amounts. Traditionally called asymmetric synthesis.
Moss, 1996
See RT **stereoselectivity**

**stereoselectivity** Specificity of chemical reactivity of stereoisomers based on their three-dimensional molecular structure.

**stochastic** Pertaining to or arising from chance and hence obeying the laws of probability.
After WHO, 1989a

**stochastic effect, stochastic process** Phenomenon pertaining to or arising from chance, and hence obeying the laws of probability.
After Duffus, 1993
RT **deterministic effect, deterministic process**

**structure activity relationship (SAR)** Association between specific aspects of molecular structure and defined biological action.
Duffus 1993
**PS quantitative structure activity relationship (QSAR)**

**structure-metabolism relationship (SMR)** Association between the physicochemical and/or the structural properties of a substance and its metabolic behaviour.

**subacute** (**effect)** See subchronic (effect)

**subchronic** Repeated over a short period, usually about 10 % of the life span; an imprecise term used to describe exposures of intermediate duration.
Duffus, 1993
RT **subchronic effect, subchronic toxicity test**

**subchronic effect** Biological change resulting from an environmental alteration lasting about 10 % of the lifetime of the test organism. In practice with experimental animals, such an effect is usually identified as resulting from multiple or continuous exposures occurring over 3 months (90 days). Sometimes a subchronic effect is distinguished from a subacute effect on the basis of its lasting for a much longer time.
Duffus, 1993
RT **subchronic toxicity test**

**subchronic toxicity test** Animal experiment serving to study the effects produced by the test substance when administered in repeated doses (or continually in food, drinking-water, air) over a period of up to about 90 days.
WHO, 1979,
SN **toxicity test**

**susceptible** Organisms that due to gender, age, physiological status, or genetic constitution are more vulnerable to a given exposure and therefore are expected to exhibit a greater response than average for the population.

**synergism** (in biology) Interaction in which the combined biological effect of two or more substances is greater than expected on the basis of the simple summation of the effect of each of the individual substances.
After Duffus, 1993
SN **synergistic effect, synergistic interaction**

**synergistic effect** (in biology) Biological effect following exposure simultaneously to two or more substances that is greater than the simple sum of the effects that occur following exposure to the substances separately.
Duffus, 1993
RT **additive effect, antagonism, potentiation**

**systemic** Relating to the body as a whole.
After Duffus, 1993
RT **systemic effect, topical**

**systemic effect** Consequence that is either of a generalized nature or that occurs at a site distant from the point of entry of a substance. A systemic effect requires absorption and distribution of the substance in the body.
Duffus, 1993
RT **local effect**

**target** (in biology) Any organism, organ, tissue, cell or cell constituent that is subject to the action of an agent.
After WHO, 1979

**three-dimensional quantitative structure-activity relationship (3D-QSAR)** Quantitative association between the three-dimensional structural properties of a substance and its biological properties.
See **quantitative structure-activity relationship**

**threshold** Dose or exposure concentration below which an effect will not occur.
After Duffus, 1993

**threshold concentration** See **threshold.**

**threshold dose** See **threshold.**

**threshold limit value®-ceiling (TLV®-C)** Concentration of a potentially toxic substance that should not be exceeded during any part of the working exposure.
ACGIH®, 2003

**threshold limit value® - time-weighted average (TLV®-TWA)** Time-weighted average concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed nearly all workers may be repeatedly exposed, day after day, without adverse effect.
ACGIH®, 2003

**threshold limit value®-short term exposure limit (TLV®-STEL)** Concentration to which it is believed that workers can be exposed continuously for a short period of time without suffering from 1) irritation, 2) chronic or irreversible tissue damage, or 3) narcosis of sufficient degree to increase the likelihood of accidental injury, impair self rescue or materially reduce work efficiency, and provided that the daily TLV®-TWA is not exceeded. It is not a separate independent exposure guideline; rather , it supplements the TLV®-TWA limit where there are recognized acute effects from a substance whose toxic effects are primarily of a chronic nature. TLV®-STELs are recommended only where toxic effects have been reported from high short-term exposures in either humans or animals.
ACGIH®, 2003

**tissue/plasma partition coefficient** See **partitioning ratio**

**tolerable daily intake (TDI)** Estimate of the amount of a potentially harmful substance (e.g., contaminant) in food or drinking water that can be ingested daily over a lifetime without appreciable health risk. (ADI is normally used for substances not known to be harmful, such as food additives)
RT **acceptable daily intake**

**tolerable weekly intake (TWI)** Estimate of the amount of a potentially harmful substance (e.g., contaminant) in food or drinking water that can be ingested weekly over a lifetime without appreciable health risk.

**topical** Substance applied directly to the surface of the body and affecting it at the point treated producing a topical effect.
RT topical effect, systemic, systemic effect.

**topical effect** Consequence of application of a substance to the surface of the body which occurs at the point of application.
RT topical, systemic, systemic effect

**toxicant** See SN **toxic substance**

**toxicity**
1. Capacity to cause injury to a living organism defined with reference to the quantity of substance administered or absorbed, the route of absorption, the distribution in time, and the specific effects produced.
2. Adverse effects of a substance on a living organism defined as in 1.
3. Measure of incompatibility of a substance with life.
After Duffus, 1993
RT **acute toxicity, chronic toxicity, subacute toxicity, subchronic toxicity.**

**toxicity equivalency factor (TEF)** Factor used in risk assessment to estimate the toxicity of a complex mixture, most commonly a mixture of chlorinated dibenzo-*p*-dioxins, furans, and biphenyls: in this case, TEF is based on relative toxicity to 2,3,7,8 -tetrachlorodibenzo-*p*-dioxin (TEF = 1).
Duffus, 1993

**toxicity equivalent (TEQ)** Contribution of a specified component (or components) to the toxicity of a mixture of related substances. The amount-of-substance (or substance concentration) of total toxicity equivalent is the sum of that for the components B, C … N:
$S\ n(TEQ) = n(TEQ)_B + n(TEQ)_C + ... n(TEQ)_N$.
Toxicity equivalent is most commonly used in relation to the reference toxicant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin by means of the toxicity equivalency factor (TEF, f) which is 1 for the reference substance. Hence:
$S\ n(TEQ) = f_B n_B + f_C n_C + ... f_N n_N$
Duffus, 1993

**toxic substance** Substance causing injury to living organisms as a result of physicochemical interactions.

**$t_{1/2}$** See **half-life, half-time**

**toxicity test** Experimental study of the adverse effects of exposure of a living organism to a substance for a defined duration under defined conditions.
After Duffus, 1993

**toxicodynamics** Process of interaction of potentially toxic substances with target sites, and the biochemical and physiological consequences leading to adverse effects.
Duffus, 1993

RT **adverse effect, pharmacodynamics, target**

**toxicogenetics** Study of the influence of hereditary factors on the effects of potentially toxic substances on individual organisms.
Duffus, 1993
RT **pharmacogenetics**

**toxicokinetics** Process of the uptake of potentially toxic substances by the body, the biotransformations they undergo, the distribution of the substances and their metabolites in the tissues, and the elimination of the substances and their metabolites from the body over a period of time.
WHO, 1979
RT **biokinetics, biotransformation, pharmacokinetics**
BT **chemobiokinetics**

**toxicologically based pharmacokinetic modelling (TBPK)** see RT **physiologically based pharmacokinetic modelling (PBPK)**

**toxicology**
1. Scientific discipline involving the study of the actual or potential danger presented by the harmful effects of substances on living organisms and ecosystems, of the relationship of such harmful effects to exposure, and of the mechanisms of action, diagnosis, prevention and treatment of intoxications.
2. Science of poisons.
Duffus, 1993

**toxin** toxic substance produced by a living organism.
PS **venom**

**tracer substance** Substance which can be tracked through one or more reactions or systems, often by detecting an incorporated isotope.

**transformed cell** Cell which has become genetically altered spontaneously or by incorporation of foreign DNA to produce a cell with an extended lifetime in culture.

**transformed cell line** See BT **cell line,** RT **transformed cell**

**transcriptomics** Global analysis of gene expression to identify and evaluate changes in synthesis of mRNA after chemical exposure.

**tubular reabsorption** Transfer of solutes from the renal tubule lumen to the tubular epithelial cell and normally from there to the peritubular fluid.

**two-compartment model** Product of compartmental analysis requiring two compartments. See RT **compartmental modelling**, BT **multicompartment analysis**

**ultrafine particles** Particles in air of aerodynamic diameters < 0.1 μm ($PM_{0.1}$)
RT **particulate matter**

**uncertainty factor (UF)**

1. In assay methodology, confidence interval or fiducial limit used to assess the probable precision of an estimate.
2. In toxicology, value used in extrapolation from experimental animals to man (assuming that man may be more sensitive) or from selected individuals to the general population. For example, a value applied to the no-observed effect level (NOEL) or no-observed adverse effect level (NOAEL) to derive an acceptable daily intake (ADI) or reference dose (RfD). The NOEL or NOAEL is divided by the value to calculate the ADI or RfD).
After Duffus, 1993
SN **modifying factor, safety factor**

**unit risk** 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 x $10^{-6}$ 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.
IRIS, 1999

**uptake** Entry of a substance into the body, into an organ, into a tissue, into a cell, or into the body fluids by passage through a membrane or by other means.
Duffus, 1993
PS **absorption**

**volume of distribution** Apparent (hypothetical) volume of fluid required to contain the total amount of a substance in the body at the same concentration as that present in the plasma assuming equilibrium has been attained.
Duffus, 1993
RT **plasma**

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

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

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);
a = fitted dose parameter (sometimes called "Weibull" parameter);
b = fitted dose parameter;
g = background response rate.
IRIS, 1999

**xenobiotic**
1. Any substance interacting with an organism that is not a natural component of that organism.
Duffus, 1993
SN **exogenous substance, foreign substance or compound**
2. Man-made compounds with chemical structures foreign to a given organism.
Nagel et al. (eds), 1991
SN **anthropogenic substance**

**zero order kinetics** Kinetics of a reaction in which the rate is independent of the concentration(s) of the reactants.
RT **equilibrium constant, rate, rate constant, kinetics**

AN antonym, opposite
BT broader term
NT narrower term
PS partial synonym
RT related term
SN exact synonym

## ANNEX 1

## ABBREVIATIONS USED IN TOXICOKINETICS

| | |
|---|---|
| **ADI** | Acceptable daily intake |
| **ALARA(P)** | As low as reasonably achievable (practicable)<br>In GBR regulations relating to worker exposure<br>In USA goal of risk management (USNRC regulations) |
| **AUC** | Area under the concentration time curve |
| **BCF** | Bioconcentration factor |
| **BEI®** | Biological Exposure Indices® (ACGIH®) |
| **BEM** | Biological effect monitoring |
| **BOD** | Biochemical oxygen demand |
| **b.w.** | Body weight |
| **$CL_n$** | See **$LC_n$** |
| **CoMFA** | Comparative Molecular Field Analysis |
| **Cyt** | Cytochrome |
| **CV** | Ceiling value |
| **$DE_n$** | See **$ED_n$** |
| **DNA** | Deoxyribonucleic acid |
| **$DN_n$** | See **$ND_n$** |
| **EC** | Enzyme classification number or effective concentration |
| **$EC_n$** | Median effective concentration to n % of a population |
| **EDI** | Estimated daily intake |
| **$ED_n$** | Median effective dose to n % of a population |
| **EEC** | Estimated exposure concentration |
| **EQS** | Environmental quality standard |
| **EED** | Estimated exposure dose |

| | |
|---|---|
| **EEL** | Environmental exposure level |
| **EMDI** | Estimated maximum daily intake |
| **GLP** | Good laboratory practice |
| **HSG** | Health and Safety Guide (IPCS) |
| **HQ** | Hazard quotient |
| **IC** | Inhibitory concentration |
| **i.c.** | Intracutaneous |
| **i.d.** | Intradermal |
| **i.m.** | Intramuscular |
| **inhl** | By inhalation |
| **i.p.** | Intraperitoneal |
| **I-TEF** | International Toxicity Equivalency Factor |
| **i.v.** | Intravenous |
| $\mathbf{K_m}$ | Michaelis constant |
| $\mathbf{K_{OC}}$ | Organic carbon partition coefficient |
| $\mathbf{K_{ow}}$ | Octanol water partition coefficient |
| **LADD** | Lifetime average daily dose |
| $\mathbf{LC_n}$ | Median concentration lethal to n % of a test population |
| $\mathbf{LC_{50}}$ | see $\mathbf{LC_n}$ |
| $\mathbf{LD_n}$ | Median dose lethal to n % of a test population |
| $\mathbf{LD_{50}}$ | see $\mathbf{LD_n}$ |
| **LEL** | Lowest effect level, same as LOEL |
| **LOEL** | Lowest observed effect level |
| **LOAEL** | Lowest observed adverse effect level |
| $\mathbf{LT_n}$ | Median time for death of n % of a test population |

| | |
|---|---|
| **LV** | Limit value |
| **MAC** | Maximum allowable concentration |
| **MEL** | Maximum exposure limit |
| **MF** | Modifying factor |
| **MOE** | Margin of exposure |
| **MPC** | Maximum permissible concentration |
| **MRL** | Maximum residue limit |
| **mRNA** | Messenger ribonucleic acid |
| **MSDS** | Material safety data sheet |
| **MTC** | Maximum tolerable concentration |
| **MTD** | Maximum tolerable dose, Maximum tolerated dose |
| **MTEL** | Maximum tolerable exposure level |
| **NADP(H)** | Nicotinamide adenine dinucleotide phosphate (reduced) |
| **$ND_n$** | Median dose narcotic to n % of a population |
| **NEL** | No effect level, same as NOEL |
| **NOAEL** | No observed adverse effect level |
| **NOEL** | No observed effect level |
| **NSC** | Normalized sensitivity coefficients |
| **PEL** | Permissible exposure limit |
| **PBPK** | Physiological Based Pharmacokinetics modelling |
| **$PM_{2.5}$** | Particles in air of with a maximum aerodynamic diameter of 2.5 µm |
| **$PM_{10}$** | Particles in air of with a maximum aerodynamic diameter of 10 µm |
| **PMR** | Proportionate mortality rate, ratio |
| **p.c.** | Per cutim (Latin) = Through the skin |

| | |
|---|---|
| **p.o.** | Per os (Latin) = By mouth |
| **POW** | Octanol water partition coefficient |
| **PPAR** | peroxisome proliferator-activated receptor |
| **PTWI** | Provisional tolerable weekly intake |
| **QSAR** | Quantitative structure activity relationship |
| **3D-QSAR** | Three-dimensional quantitative structure-activity relationship |
| **QSMR** | Quantitative structure metabolism relationship |
| **RD** | Rate difference |
| **RfC** | Reference concentration |
| **RfD** | Reference dose |
| **RNA** | Ribonucleic acid |
| **RR** | Rate ratio |
| **ROS** | Reactive oxygen species |
| **SAR** | Structure-activity relationship |
| **s.c.** | Subcutaneous |
| **SCE** | Sister chromatid exchange |
| **SMR** | Standard mortality ratio |
| **SMR** | Structure metabolism relationship |
| **SNARL** | Suggested no adverse response level |
| **STEL** | Short term exposure limit |
| **$t_{1/2}$** | Half-life, half time |
| **TBPK** | Toxicologically based pharmacokinetic modelling |
| **TCDD** | 2,3,7,8-tetrachlorodibenzo-p-dioxin |
| **TDI** | Tolerable daily intake |
| **TEF** | Toxicity equivalency factor |

| | |
|---|---|
| **TEQ** | Toxicity equivalent |
| **$TL_n$** | See $LT_n$ |
| **TLV®** | Threshold limit value® (ACGIH®) |
| **TMDI** | Theoretical maximum daily intake |
| **TWA** | Time-weighted average |
| **TWAC** | Time-weighted average concentration |
| **TWAE** | Time-weighted average exposure |
| **TWI** | Tolerable weekly intake |
| **UF** | Uncertainty factor |
| **$V_{max}$** | Maximum velocity |

## ANNEX 2

## ABBREVIATIONS OF INTERNATIONAL BODIES AND LEGISLATION

| | |
|---|---|
| **ACGIH®** | American Conference of Governmental Industrial Hygienists |
| **ATSDR** | Agency for Toxic Substances and Diseases Registry |
| **BCR** | Bureau Communautaire de Référence (Bruxelles) |
| **BIBRA** | British Industrial Biological Research Association |
| **CCFA** | Codex Committee on Food Additives |
| **CCPR** | Codex Committee on Pesticide Residues |
| **CDC** | Centers for Disease Control and Prevention |
| **CEC** | Commission of the European Communities |
| **CERCLA** | Comprehensive Environmental Response, Compensation, and Liability Act (USA) |
| **CHIP** | Classification, Hazard Information and Packaging (GBR) |
| **COSHH** | Control of Substances Hazardous to Health Regulations (GBR) |
| **CPL** | Classification, Packaging and Labelling |
| **EC** | European Community, European Commission |
| **ECB** | European Chemicals Bureau |
| **EEA** | European Environmental Agency |
| **EEC** | European Economic Community |
| **EINECS** | European Inventory of Existing Chemical Substances |
| **ELINCS** | European List of New Chemical Substances |
| **EPA** | Environmental Protection Agency (USA), same as USEPA |
| **EUROTOX** | European Society of Toxicology |
| **EUSES** | European Uniform System for Evaluation of Substances |
| **FAO** | Food and Agricultural Organization |

| | |
|---|---|
| **FDA** | Food and Drug Administration (USA) |
| **IAEA** | International Atomic Energy Agency |
| **IARC** | International Agency for Research on Cancer |
| **ICH** | International Conference for Harmonization |
| **ICRP** | International Commission on Radiological Protection |
| **ICSU** | International Council of Scientific Unions |
| **IFCC** | International Federation of Clinical Chemists |
| **ILO** | International Labour Organization |
| **IPCS** | International Programme on Chemical Safety, UNEP, ILO, WHO |
| **IRIS** | Integrated Risk Information System (USA) |
| **IRPTC** | International Register of Potentially Toxic Chemicals, now UNEP Chemicals |
| **ISO** | International Organization for Standardization |
| **IUPAC** | International Union of Pure and Applied Chemistry |
| **IUTOX** | International Union of Toxicology |
| **JECFA** | Joint FAO/WHO Expert Committee on Food Additives |
| **JMPR** | Joint FAO/WHO Meeting on Pesticide Residues |
| **NBS** | National Bureau of Standards (USA), now NIST |
| **NIH** | National Institutes of Health (USA) |
| **NIOSH** | National Institute of Occupational Safety & Health (USA) |
| **NIST** | National Institute of Standards and Technology (USA), formerly NBS |
| **NRC** | National Research Council (USA) |
| **OECD** | Organization for Economic Cooperation and Development |
| **OMS** | Organisation Mondiale de la Santé, same as WHO |
| **OSHA** | Occupational Safety and Health Administration (USA) |

**RSC** The Royal Society of Chemistry (GBR)

**SCOPE** Scientific Committee on Problems of the Environment (ICSU)

**TOSCA** Toxic Substances Control Act (USA)

**UNEP** United Nations Environment Programme

**USEPA** United States Environmental Protection Agency, same as EPA

**WHO** World Health Organization, same as OMS

## ANNEX 3

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