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GLOSSARY OF TERMS USED IN TOXICOKINETICS

(IUPAC Recommendations 2003)

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Glossary of terms used in toxicokinetics

(IUPAC Recommendations 2003)

Abstract: This glossary contains definitions of 365 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. Some medical terms are included, where relevant, 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 and acronyms used in toxicokinetics, one containing a list of abbreviations and acronyms of names of international bodies and legislation that are relevant to toxicology and chemical safety, and one giving sources 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. 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 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. Furthermore, 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 have 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. The names are listed below. 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.

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ALPHABETICAL ENTRIES

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 [20,38]

Synonym: *internal dose*

absorbed dose (of radiation), *D*

Energy imparted by ionizing radiation to a specified volume of matter divided by the mass of that volume.

After [31,38]

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 the number of organisms used in its assessment.

[38]

absorptance (in chemistry), α

Ratio of the absorbed to the incident radiant power. Also called *absorption factor*. When $\alpha \leq 1$, $\alpha \approx A_e$, where A_e is the Napierian absorbance.

[38]

absorption (general)

1. Process of one material (the absorbent) being retained by another (the absorbate).

Note: The process may be the physical dissolution of a gas, liquid, or solid in a liquid, a gas or liquid in a solid, attachment of molecules of a gas, vapor, liquid, or dissolved substance to a solid surface by physical forces, etc.

2. Transfer of some or all of the energy of radiation to matter which it traverses.

Note: Absorption of light at bands of characteristic wavelengths is used as an analytical method in spectrophotometry to identify the chemical nature of molecules, atoms, or ions and to measure the concentrations of these species.

Modified from [38]

absorption (in biology)

Penetration of a substance into an organism by various processes, some specialized, 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 [20]

absorption (of radiation)

Phenomenon in which radiation transfers some or all of its energy to matter which it traverses.

[31]

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 quantity (*uptake*) of a substance to the administered quantity (intake).

Note: For exposure by way of the respiratory tract, the absorption coefficient is the ratio of the absorbed quantity to the quantity of the substance (usually particles) deposited (adsorbed) in the lungs.

[30]

Synonym: *absorption factor*

absorption factor

See preferred synonyms *absorptance* (in chemistry), *absorption coefficient* (in biology).

acceptable daily intake, ADI

Estimate by JECFA of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health *risk*.

Note 1: For calculation of ADI, a standard body mass of 60 kg is used.

Note 2: Tolerable daily intake (TDI) is the analogous term used for contaminants.

[38,67]

accumulation (in biology)

See *bioaccumulation*.

activation (in biology)

See *bioactivation*.

active metabolite

Metabolite with biological and/or toxicological activity.

See also *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 [20]

Antonym: *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 [20]

acute exposure

Exposure of short duration.

See also *acute*, *exposure*.

Antonym: *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 [20]

Antonym: *chronic toxicity*

additive effect

Consequence that follows *exposure* to two or more physicochemical agents which act jointly but do not interact: the total effect is the simple sum of the effects of separate exposures to the agents under the same conditions.

[20]

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 [38]

See also *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*.

advection (in environmental chemistry)

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 [59]

aerodynamic diameter (of a particle)

Diameter of a spherical particle with relative density equal to unity, which has the same settling velocity in air as the particle in question.

After [28]

aerosol

Mixtures of small particles (solid, liquid, or a mixed variety) and the *carrier* gas (usually air).

Note 1: Owing to their size, these particles (usually less than 100 μm and greater than 0.01 μm in diameter) have a comparatively small settling velocity and hence exhibit some degree of stability in the earth's gravitational field.

Note 2: An aerosol may be characterized by its chemical composition, its radioactivity, the particle size distribution, the electrical charge, and the optical properties.

[38]

aliquot (in analytical chemistry)

Known amount of a homogeneous material, assumed to be taken with negligible *sampling error*.

Note 1: The term is usually applied to fluids.

Note 2: The term "aliquot" is usually used when the fractional part is an exact divisor of the whole; the term "aliquant" has been used when the fractional part is not an exact divisor of the whole (e.g., a 15-ml portion is an aliquant of 100 ml).

Note 3: When an aliquot is taken of a laboratory sample or test sample or the sample is otherwise subdivided, the samples have been called split samples.

[38]

allometric

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

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, α = growth coefficient of the organ, and b = a constant.

[45]

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 [19]

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.

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 *effect* is produced by *exposure* to either of two factors, but not by exposure to both together.

[20,38]

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 without associated inflammation.

See also *necrosis*.

area under the concentration-time curve

See *area under the curve*.

area under the curve, AUC

Area between a curve and the horizontal axis, 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.

area under the moment curve, AUMC

Area between a curve and the horizontal axis in a plot of (*concentration* \times time) vs. time.

attributable risk

Part of a *risk* that is identified as due to *exposure* to a defined substance.

After [35]

autooxidation

Self-catalyzed oxidation reaction that occurs spontaneously in an aerobic environment.

Bateman function

Equation expressing the build-up and decay in *concentration* of a substance (usually in *plasma*) based on first-order *uptake* and *elimination* in a *one-compartment model*, having the form

$$C = [fDk_a/V(k_a - k_e)][\exp(-k_e t) - \exp(-k_a t)]$$

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 [29]

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 [29]

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. [71]

benchmark response

Response expressed as an excess of background, at which a *benchmark dose* or *benchmark concentration* is set.

After [29]

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.

See also *bioconcentration*, *biomagnification*.

bioactivation

Metabolic *conversion* of a *xenobiotic* to a more *toxic* derivative.

[20]

bioassay

Procedure for estimating the *concentration* or biological activity of a substance by measuring its effect on a living system compared to a standard system.

Modified from [38,42]

bioavailability (general)

Extent of *absorption* of a substance by a living organism compared to a standard system.

Synonyms: *biological availability*, *physiological availability*

bioavailability (in pharmacokinetics)

Ratio of the *systemic exposure* from extravascular (ev) *exposure* to that following intravenous (iv) exposure as described by the equation:

$$F = A_{\text{ev}} D_{\text{iv}} / B_{\text{iv}} D_{\text{ev}}$$

where F is the *bioavailability*, A and B are the *areas under the* (plasma) *concentration-time curve* following extravascular and intravenous administration respectively, and D_{ev} and D_{iv} are the administered extravascular and intravenous *doses*.

After [20]

bioconcentration

Process leading to a higher *concentration* of a substance in an organism than in environmental media to which it is exposed.

After [51]

See also *bioaccumulation*.

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 [53]

bioconjugate

See *conjugate*.

bioconversion

See synonym *biotransformation*.

bioinactivation

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

biokinetics (in toxicology)

Science of the movements involved in the *distribution* of substances.

After [19]

biological assessment of exposure

See *biological monitoring*.

biological exposure indices, BEI

Guidance value recommended by ACGIH for assessing *biological monitoring* results.

biological half life

For a substance, the time required for the amount of that substance in a biological system to be reduced to one half of its value by biological processes, when the rate of removal is approximately exponential. [38]

biological half time, $t_{1/2}$

See *biological half life*.

biological monitoring

Continuous or repeated measurement of potentially *toxic substances* or their *metabolites* or biochemical effects in tissues, secretions, 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*.

[20]

Synonym: *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.

Note: Such an indicator may be a measurable chemical, biochemical, physiological, behavioral, or other alteration within an organism.

[20]

biomarker of effect

Biomarker that, depending on its magnitude, can be recognized as associated with an established or possible health impairment or disease.

[68]

biomarker of exposure

Biomarker that relates *exposure* to a *xenobiotic* 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.

[68]

biomarker of susceptibility

Biomarker of an inherent or acquired ability of an organism to respond to *exposure* to a specific substance.

[68]

biomonitoring

See synonym *biological monitoring*.

biotransformation

Chemical conversion of a substance that is mediated by living organisms or enzyme preparations derived therefrom.

[38,42]

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 [19]

blood plasma

See *plasma* (in biology).

body burden

Total amount of a substance present in an organism at a given time.

After [20]

carcinogen n., -ic adj.

Agent (chemical, physical, or biological) which is capable of increasing the *incidence* of malignant neoplasms.

[26]

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.

[38]

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 [57]

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 [10].
4. Protein found in cell membranes, which facilitates transport of a ligand across the membrane.

carrier substance

Substance which binds to another substance and transfers it from one site to another.

ceiling value, CV

Airborne *concentration* of a potentially *toxic substance* which should never be exceeded in a worker's breathing zone.

After [20]

cell line

Defined unique population of cells obtained by culture from a primary source through numerous generations.

After [20]

See also *transformed cell line*.

chemical conversion

Change from one *chemical species* to another.

After [20]

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.

[52]

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.

Antonym: *acute*

chronic effect

Consequence that develops slowly and/or has a long lasting course: may be applied to an effect that develops rapidly and is long lasting.

After [61]

Antonym: *acute effect*

Synonym: *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 lifetime.

[20]

Antonym: *acute exposure*

Synonym: *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.

[20]

Antonym: *acute toxicity*

chronotoxicology

Study of the influence of biological rhythms on the *toxicity* of substances.

[20]

clearance (general), $(c_o/c_i)(\Delta V/\Delta t)$

Product of the *concentration* c_o of a component in an output system and the volume flow rate of the output system divided by the concentration c_i of this component in the input system.

Note: The term "mean volume rate" is recommended for this quantity.

[38]

clearance (in toxicology)

1. Volume of blood or *plasma* or mass of an organ effectively cleared of a substance by *elimination* (*metabolism* and *excretion*) divided by time of elimination.

Note: Total clearance is the sum of the clearances of each eliminating organ or tissue for a given substance.

2. (in *pulmonary toxicology*) Volume or mass of lung cleared divided by time of *elimination*; used qualitatively to describe removal of any inhaled substance which deposits on the lining surface of the lung.
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*.

[20]

comparative risk

See *relative excess risk*.

compartment

Conceptualized part of the body (organs, tissues, cells, or fluids) considered as an independent system for purposes of modeling and assessment of *distribution* and *clearance* of a substance.

After [61]

compartmental analysis

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

$$C = Ae^{-\alpha t} + Be^{-\beta t} \dots$$

where each exponential term represents one compartment. *C* is the substance *concentration*; *A*, *B*, ... are proportionality constants; α , β , ... are rate constants; and *t* is time.

concentration

1. Any one of a group of three quantities characterizing the composition of a mixture and defined as one of mass, amount of substance (chemical amount), or number divided by volume, giving, respectively, mass, amount (of substance), or number concentration.
2. Short form for amount (of substance) concentration (substance concentration in clinical chemistry).

Modified from [38]

concentration–effect curve

Graph of the relation between *exposure concentration* and the magnitude of the resultant biological change.

[20]

Synonym: *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 [20]

concentration–response curve

Graph of the relation between *exposure concentration* and the proportion of individuals in a population responding with a defined effect.

After [20]

concentration–response relationship

Association between *exposure concentration* and the *incidence* of a defined effect in an exposed population.

After [20]

congener

One of two or more substances related to each other by origin, structure, or function.

After [20]

conjugate

1. Molecular species produced in living organisms by covalently linking two chemical moieties from different sources.

Example: A conjugate of a *xenobiotic* with some group such as glutathione, sulfate or glucuronic acid, making it soluble in water or *compartmentalized* within the cell.

[38]

See also *phase II reaction*.

2. Material produced by attaching two or more substances together, e.g., a *conjugate* of an antibody with a fluorochrome or enzyme.

After [20]

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 [38]

conversion

See *chemical conversion*, *biotransformation*.

count mean diameter

Mean of the diameters of all particles in a population.

[65]

See also *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.

[65]

See also *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.

[20]

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 [65]

critical end-point

Toxic effect used by the USEPA as the basis for a *reference dose*.

[5]

critical group

Part of a *target* population most in need of protection because it is most *susceptible* to a given *toxicant*.

[61]

critical organ (in toxicology)

Organ that attains the *critical concentration* of a substance and exhibits the *critical effect* under specified circumstances of *exposure* and for a given population.

After [20]

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.

[20]

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 [20]

critical study

Investigation yielding the no observed *adverse effect* level that is used by the USEPA as the basis of the *reference dose*.

[5]

Synonym: *pivotal study*

cumulative effect

Overall change which occurs after repeated *doses* of a substance or radiation.

After [20]

cumulative incidence

Number or proportion of individuals in a group who experience the onset of a health-related event during a specified time interval.

Note: 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 [35]

Synonym: *incidence proportion*

cumulative incidence rate

Proportion of the *cumulative incidence* to the total population.

After [35]

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 [20]

cytochromes

Conjugated proteins containing haem as the *prosthetic group* and associated with electron transport and with redox processes.

[38]

cytochrome P450

Member of a superfamily of heme-containing monooxygenases 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 the presence of a thiolate in the axial position of the heme opposite to the carbon monoxide ligand.

deterministic effect, deterministic process

Phenomenon committed to a particular outcome determined by fundamental physical principles.

See also *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.

[20,38]

diffusion

Spontaneous differential movement of components in a system.

Note: In molecular terms, the driving force for diffusion is random thermal motion. In thermodynamic terms, the driving force is a gradient of chemical potential.

diffusion coefficient, D

Proportionality constant D , relating the flux of amount (J_n) of entities B to their *concentration* gradient

$$J_n = -D \text{ grad } c_B$$

[38]

dispersion (in environmental chemistry)

Dilution of a pollutant by spreading in the atmosphere or water due to *diffusion* or turbulent action.

After [38]

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.
[20]
2. Total of the processes of *absorption* of a chemical into the circulatory systems, *distribution* throughout the body, *biotransformation*, and *excretion*.

distribution

1. Apportionment of a solute between two phases. The terms “partition” or “extraction” may also be used in this sense where appropriate.
[38]
2. Dispersal of a substance and its derivatives throughout the natural environment or throughout an organism.
3. Final location(s) of a substance within an organism after dispersal.

After [20]

distribution constant

See *partition ratio*,

distribution volume

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

dominant half life

Half life of a fraction of a substance in a specific organ or *compartment* if it defines approximately the overall *clearance* rate for that substance at a specific time point.

dosage

Dose divided by product of mass of organism and duration of dose.

Note: Often expressed $\text{mg (kg body weight)}^{-1} \text{ day}^{-1}$ and may be used as a synonym for dose.

[20]

dose (of a substance)

Total quantity of a substance administered to, taken up, or absorbed by an organism, organ, or tissue.

After [20]

dose (of radiation)

Energy or amount of photons absorbed by an irradiated object during a specified *exposure* time divided by area or volume.

After [38]

dose–effect

Relation between *dose* and the magnitude of a measured biological change.

dose–effect curve

Graph of the relation between *dose* and the magnitude of the biological change produced measured in appropriate units.

[20]

dose–effect relationship

Association between *dose* and the resulting magnitude of a continuously graded change, either in an individual or in a population.

After [20]

dose–response curve

Graph of the relation between *dose* and the proportion of individuals in a population responding with a defined biological effect.

[20]

dose–response relationship

Association between *dose* and the *incidence* of a defined biological effect in an exposed population usually expressed as percentage.

After [20]

elimination (in toxicology)

Disappearance of a substance from an organism or a part thereof, by processes of *metabolism*, secretion, or *excretion*.

After [61]

See also *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*.

endocytosis

Uptake of material into a cell by invagination of the *plasma* membrane and its internalization in a membrane-bounded vesicle.

[3]

See also *phagocytosis*, *pinocytosis*.

endogenous

Produced within or caused by factors within an organism.

endothelium

Layer of flattened epithelial cells lining the heart, blood vessels, 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 [20]

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*.

[20]

enzyme induction

Process whereby an enzyme is synthesized in response to the presence of a specific substance or to other agents such as heat or a metal.

Modified from [38]

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 in which the defining variables (temperature, pressure, chemical potential) have constant values.

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, feces, or other products normally leaving the body.

Note: Excretion does not include the passing of a substance through the intestines without *absorption*.

After [65]

See also *clearance*, *elimination*.

excretion rate

Amount of substance and/or its *metabolites* that is excreted divided by time of *excretion*.

[20]

exogenous substance

See preferred synonym: *xenobiotic*.

exponential decay

Variation of a quantity according to the law

$$A = A_0 e^{-\lambda t}$$

where A and A_0 are the values of the quantity being considered at time t and zero respectively, and λ is an appropriate positive constant.

[38]

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 concentration, duration, and frequency (for chemical agents and microorganisms) or intensity (for physical agents).

[20]

2. Process by which a substance becomes available for *absorption* by the *target* population, organism, organ, tissue, or cell, by any route.

[20]

3. For X- or γ -radiation in air, the sum of the electrical charges of all the ions of one sign produced when all electrons liberated by photons in a suitably small element of volume of air completely stopped, divided by the mass of the air in the volume element.

[38]

exposure assessment

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

[20]

exposure–effect curve

See *concentration–effect curve*.

extracellular space

Volume within a tissue, outside cells, and excluding vascular and lymphatic space.

extracellular volume

Volume of fluid outside the cells but within the outer surface of an organism.

extraction ratio

Amount of substance extracted from a source divided by the total contained within the source.

first-order process

1. Chemical reaction where the *rate* is directly proportional to the *concentration* of reactant.

[10]

2. Any reaction changing at a constant fractional *rate*.

Synonym: *first-order reaction*

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 [20]

first-pass metabolism

See *first-pass effect*.

foreign substance

See preferred synonym: *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.

[52]

gavage

Administration of materials directly into the stomach by oesophageal intubation.

[20]

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.

genotoxic

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

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 [42]

glomerulus

Tuft or a cluster, as of a plexus of capillary blood vessels or nerve fibers, e.g., capillaries of the filtration apparatus of the kidney.

After [20]

glomerular filtration

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

glomerular filtration rate

Volume of ultrafiltrate formed in the kidney tubules from the blood passing through the glomerular capillaries divided by time of filtration.

half life, $t_{1/2}$

Time required for the *concentration* of a reactant in a given reaction to reach a value that is the arithmetic mean of its initial and final (equilibrium) values. For a reactant that is entirely consumed, it is the time taken for the reactant concentration to fall to one half its initial value.

Note: The half life of a reaction has meaning only in special cases:

1. For a first-order reaction, the half life of the reactant may be called the half life of the reaction.
2. For a reaction involving more than one reactant, with the *concentrations* of the reactants in stoichiometric ratios, the half life of each reactant is the same, and may be called the half life of the reaction.

If the concentrations of reactants are not in their stoichiometric ratios, there are different half lives for different reactants, and one cannot speak of the half life of the reaction.

Modified from [38]

Synonym: *half time*

half time, $t_{1/2}$

See synonym: *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.

[20]

See also *risk*.

Henderson–Hasselbach equation

Equation of the form:

$$\text{pH} = \text{p}K_{\text{a}} - \lg([\text{HA}]/[\text{A}^-])$$

for the calculation of the pH of solutions where the ratio $[\text{HA}]/[\text{A}^-]$ is known and HA and A^- are the protonated and deprotonated forms of an acid, respectively.

[38]

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 $\lg[\theta/(1-\theta)]$ vs. $\lg[\text{A}]$ has a slope of 1 if binding is noncooperative and >1 if binding is cooperative.

$$\theta = [\text{A}]_{\text{bound}}/n[\text{P}]_{\text{total}} \text{ is the fraction of sites occupied.}$$

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*.

Note: When expressed as a *rate*, it is the number of ill persons divided by the average number of persons in the specified population during a defined period, or alternatively divided by the estimated number of persons at the midpoint of that period.

[65]

infusion (in physiology)

Therapeutic introduction of a fluid other than blood, as a (usually saline) solution, into a vein.

After [19]

interfacial layer

Inhomogeneous region intermediate between two bulk phases in contact, and where properties are significantly different from, but related to, the properties of the bulk phases.

[38]

internal dose

See preferred synonym: *absorbed dose*.

interstitial fluid

Aqueous solution filling the narrow spaces between cells.

intrinsic activity

Maximal stimulatory effect induced by a compound in relation to that of a given reference compound.
After [57]

intrinsic clearance

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

intrinsic factor (in biochemistry)

Specific protein required for the *absorption* of vitamin B₁₂ 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 [16]

latency

See synonym: *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 [20]

lethal concentration, LC

Concentration of a substance in an environmental medium that causes death following a certain period of *exposure*.
[38]

lethal dose, LD

Amount of a substance or physical agent (e.g., radiation) that causes death when taken into the body.
After [20,38]

lethal synthesis

Metabolic formation of a highly *toxic* compound often leading to death of affected cells.
After [20,38]

linearized multistage model

Sequence of steps in which (a) a *multistage model* is fitted to *tumor 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*.
[20]

local effect

Change occurring at the site of contact between an organism and a *toxicant*.
[20]

logit

In competitive binding assays, the *logit-log dose* relationship, in which the *response* is defined by:

$$R = \text{logit}(y) = \lg [y/(1 - y)]$$

where $y = b/b_0$ with b = fraction of tracer bound and b_0 = value of b with no unlabeled ligand in the system.

Note: Logit transformed assay data frequently yield straight-line dose–response data, amenable to statistical analysis. More generally in toxicology, the transformation is applied to dose–response data, where b_0 denotes the maximum response in the absence of a toxic substance.

Modified from [38]; see also [20]

log-normal distribution

Distribution function $F(y)$, in which the logarithm of a quantity is normally distributed, i.e.,

$$F(y) = f_{\text{gauss}}(\ln y)$$

where $f_{\text{gauss}}(x)$ is a Gaussian *distribution*.
[38]

log-normal transformation

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

long-term effect

See synonym: *chronic effect*.

long-term exposure

See synonym: *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 *minimum lethal concentration*.

lowest-observed-adverse-effect level, LOAEL

Lowest *concentration* or amount of a substance (*dose*), found by experiment or observation, which causes an *adverse effect* on 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*.

[38]

lowest-observed-effect level, LOEL

Lowest *concentration* or amount of a substance (*dose*), 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*.

[20,38]

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 defense mechanisms.

[20]

margin of exposure, MOE

Ratio of the no-observed-adverse-effect level (NOAEL) to the theoretical or estimated *exposure dose* (EED) or *concentration* (EEC).

[20]

margin of safety, MOS

See synonym: *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.

[20]

mass median diameter

Diameter of a spherical particle with the median mass of all the particles in a population.

[25]

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).

[20,38]

maximum tolerable dose, MTD

Highest amount of a substance that, when introduced into the body, does not kill test animals (denoted by LD_0).

[20,38]

maximum tolerable exposure level, MTEL

Maximum amount (*dose*) or *concentration* of a substance to which an organism can be exposed without leading to an *adverse effect* after prolonged *exposure* time.

[20,38]

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.

Note: 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.

Note: In some studies, toxicity that could interfere with a carcinogenic effect is specifically excluded from consideration.

[20,38]

maximum velocity (maximum rate), V_{\max}

In *Michaelis–Menten kinetics*, the maximum rate of *conversion* of a substrate when its *concentration* is not rate limiting.

Synonym: maximum rate.

mean residence time, MRT (in pharmacokinetics)

Average time a drug molecule remains in the body or an organ after rapid intravenous injection.

Note 1: Like clearance, its value is independent of dose.

Note 2: After an intravenous bolus:

$$t_r = A_m / A$$

where t_r is the MRT, A is the area under the plasma concentration-time curve, and A_m is the area under the moment curve.

Note 3: For a drug with one-compartment distribution characteristics, MRT equals the reciprocal of the elimination rate constant.

After [6]

median effective concentration, EC_{50}

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.

[20,38]

median effective dose, ED_{50}

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.

[20,38]

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.

[20,38]

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.

[20,38]

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.

[20,38]

metabolic activation

Biotransformation of a substance to a more biologically active derivative.

Synonym: *bioactivation*

metabolic enzymes

Proteins that catalyze chemical transformations of body constituents and, in more common usage, of *xenobiotics*.

metabolic half life, metabolic half time

Time required for one half of the quantity of a substance in the body to be metabolized.

Note: This definition assumes that the final quantity in the body is zero. See the definition of *half life*.

After [20]

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 (see *elimination*) by different organs as unchanged substance or *metabolites*.

[65]

metabolic transformation

Biotransformation of a substance that takes place within a living organism.

After [20]

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.

Note: It includes the uptake and distribution within the body of a substance, the changes (*biotransformation*) undergone by such a substance, and the *elimination* of the substance and of its *metabolites*.

[65]

metabolite

Intermediate or product resulting from *metabolism*.

After [38]

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

Substance *concentration* of substrate at which the rate of reaction is equal to one half of the limiting rate (maximum rate). Also called the Michaelis *concentration*. The *Michaelis constant* (Michaelis concentration) may be used only when Michaelis–Menten *kinetics* is obeyed.

[38]

Michaelis–Menten kinetics

Dependence of an initial rate of reaction upon the total *concentration* of a substrate S that is present in large excess over the *concentration* of an enzyme or other catalyst (or reagent) E with the appearance of saturation behavior following the Michaelis–Menten equation:

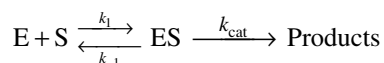
$$v = V[S]_0 / (K_M + [S]_0)$$

where v is the observed initial rate, V is its limiting value at substrate saturation (i.e., $[S]_0 \gg K_M$), and K_M the substrate *concentration* when $v = V/2$. The definition is experimental, i.e., it applies to any reaction that follows an equation of this general form. The symbols V_{\max} or v_{\max} are sometimes used for V .

Note 1: The parameters V and K_M (the ‘*Michaelis constant*’) of the equation can be evaluated from the slope and intercept of a linear plot of $1/v$ vs. $1/[S]_0$ (‘Lineweaver–Burk plot’) or from slope and intercept of a linear plot of v vs. $v/[S]_0$ (‘Eadie–Hofstee plot’).

Note 2: A Michaelis–Menten equation is also applicable to the condition where E is present in large excess, in which case the total *concentration* $[E]_0$ appears in the equation instead of $[S]_0$.

Note 3: The term has sometimes been used to describe reactions that proceed according to the scheme:

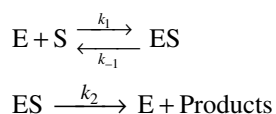


in which case, $K_M = (k_{-1} + k_{\text{cat}})/k_1$ (Briggs–Haldane conditions). It has more usually been applied only to the special case in which $k_{-1} \gg k_{\text{cat}}$ and $K_M = k_{-1}/k_1 = K_S$, the dissociation constant of the complex. In this case, K_M is a true dissociation constant (Michaelis–Menten conditions).

From [38] with a more logical symbol for the *Michaelis constant*, and with notation consistent with *Michaelis–Menten mechanism*.

Michaels–Menten mechanism

Michaelis–Menten mechanism is the simplest mechanism that will explain *Michaelis–Menten kinetics*. According to the mechanism, a substrate S first combines with a molecule of enzyme E, and this process is followed by a step in which the enzyme–substrate complex ES breaks down (sometimes with the participation of the solvent) into enzyme and reaction products:



If, as is usual, the substrate S is present in great excess of the enzyme, it can be shown that steady-state conditions apply, and that the rate equation is:

$$v = \frac{k_2[E]_0[S]_0}{(k_{-1} + k_1) / k_1 + [S]_0}$$

where $[E]_0$, $[S]_0$ are the total *concentrations* of enzyme and substrate. This equation is of the required general form of the Michaelis–Menten equation.

Note: Other, more complicated, mechanisms lead to the Michaelis–Menten equation, adherence to which, therefore, does not require that the Michaelis–Menten mechanism applies.

From [38], with symbols consistent with those in *Michaelis–Menten kinetics*.

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.

[38,61]

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.

Note: Evaluation requires comparison with appropriate reference values based on knowledge of the probable relationship between ambient *exposure* and *adverse effects*.

After [7,62,72]

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*.

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

$$P = 1 - \exp[-(q_0 + q_1d_1 + q_2d_2 + \dots + q_kd_k)]$$

where P is the probability of cancer death from a continuous *dose rate*, d_i , of group (or stage) i , 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.

[20]

Multivariate statistics

Set of statistical tools to analyze data matrices using regression and/or pattern recognition techniques.

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 [20]

Necrosis

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

See also *apoptosis*.

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.

[20]

No-effect level, NEL

Maximum *dose* (of a substance) that produces no detectable changes under defined conditions of *exposure*.

Note: This term tends to be substituted by no-observed-adverse-effect level (NOAEL) or no-observed-effect level (NOEL).

[20]

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*.

[38,61]

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*.

[20,38]

One-compartment model

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

[63]

one-hit model

Dose–response model of the form

$$P = 1 - e^{-bd}$$

where P is the probability of cancer death from a continuous *dose* rate, d , and b is a constant.

[20]

particulate matter (in atmospheric chemistry)

1. General term used to describe airborne solid or liquid particles of all sizes.

Note: The term *aerosol* is recommended to describe airborne particulate matter.

[38]

2. 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 [70]

partition coefficient

Concentration of a substance in one phase divided by the concentration of the substance in the other phase when the heterogeneous system of two phases is in *equilibrium*.

Note 1: The ratio of concentrations (or, strictly speaking, activities) of the same molecular species in the two phases is constant at constant temperature.

Note 2: The octanol/water partition coefficient is often used as a measure of the *bioconcentration* factor for modeling purposes.

After [20]

Note 3: This term is in common usage in toxicology but is not recommended by IUPAC for use in chemistry and should not be used as a synonym for partition constant, partition ratio, or distribution ratio.

[38]

partition ratio, K_D

Ratio of the *concentration* of a substance in a single definite form, A , in the extract to its concentration in the same form in the other phase at equilibrium, e.g., for an aqueous/organic system:

$$K_D(A) = [A]^{\text{org}}/[A]^{\text{aq}}$$

[38]

perfusion (in physiology)

1. 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.

[19]

phagocytosis

Process by which particulate material is endocytosed by a cell.

[3]

See also *endocytosis*, *pinocytosis*.

pharmacodynamics

Process of interaction of pharmacologically active substances with *target* sites in living systems, and the biochemical and physiological consequences leading to therapeutic or *adverse effects*.

Corrected from [38]; see also [20].

pharmacogenetics

Study of the influence of genetic factors on the effects of drugs on individual organisms.

After [20]

pharmacokinetics

1. Process of the *uptake* of drugs by the body, the *biotransformation* 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.
2. Study of such processes.

After [20,38]

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 catalyzed by enzymes of the cytosol, of the endoplasmic reticulum (microsomal enzymes) or of other cell organelles.

[20]

See also *cytochrome P450*.

phase II reaction (of biotransformation)

Binding of a substance, or its *metabolites* from a phase I reaction, with *endogenous* molecules (*conjugation*), making more water-soluble derivatives that may be excreted in the urine or bile.

[20]

phase III reaction (of biotransformation)

Further *metabolism* of *conjugated metabolites* produced by *phase II reactions*.

After [20]

phenotype

Observable structural and functional characteristics of an organism determined by its *genotype* and modulated by its environment.

[38,42]

physiological availability

See *bioavailability*.

physiological pharmacokinetic model

See *physiologically based pharmacokinetic modeling*.

physiologically based pharmacokinetic modeling, PBPK

Mathematical modeling of kinetic behavior of a substance, based on measured physiological parameters.

Synonym: *toxicologically based pharmacokinetic modeling*

pinocytosis

Type of *endocytosis* in which soluble materials are taken up by the cell and incorporated into vesicles for digestion.

After [3]

pivotal study

See synonym: *critical study*.

plasma (in biology)

1. Fluid component of blood in which the blood cells and platelets are suspended.

Synonym: *blood plasma*

[20]

2. Fluid component of semen produced by the accessory glands, the seminal vesicles, the prostate, and the bulbo-urethral glands

[20]

3. Cell substance outside the nucleus, i.e., the cytoplasm.

[20]

poison (in toxicology)

Substance that, taken into or formed within the organism, impairs the health of the organism and may kill it.

After [20]

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*.

[61]

potency (in toxicology)

Expression of relative *toxicity* of an agent as compared to a given or implied standard or reference.

After [20]

potentiation

Dependent action in which a substance or physical agent at a *concentration* or *dose* that does not itself have an *adverse effect* enhances the harm done by another substance or physical agent.

[20,38]

procarcinogen

Substance that has to be metabolized before it becomes a *carcinogen*.

After [20]

prodrug

Precursor converted to an active form of a drug within the body.

prosthetic group

Non-protein entity essential for an enzyme's activity and tightly bound to the enzyme molecule in its active form.

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.

Note: 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 lung(s).

quantal

Describing a condition that can be expressed only as occurring or not occurring, such as death.

After [20]

quantitative structure–activity relationships, QSAR

Quantitative structure–biological activity models derived using *regression analysis* and containing as parameters physicochemical constants, indicator variables, or theoretically calculated values.

Note: The term is extended by some authors to include chemical reactivity, i.e., activity and reactivity are regarded as synonyms. The extension is discouraged.

Modified from [38]; see also [20].

quantitative structure–metabolism relationship, QSMR

Quantitative association between the physicochemical and/or the structural properties of a substance and its metabolic behavior.

rate (in epidemiology)

Measure of the frequency with which an event occurs in a defined population in a specified period of time.

Note 1: Most such rates are ratios, calculated by dividing a numerator, e.g., the number of deaths, or newly occurring cases of a disease in a given period, by a denominator, e.g., the average population during that period.

Note 2: Some rates are proportions, i.e., the numerator is contained within the denominator.

After [35]

rate constant, k

Proportionality that relates the *rate* of a chemical reaction to some function of reactant *concentrations*.

After [40]

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 O₂ to water.

Examples: superoxide O₂^{-•}, hydrogen peroxide H₂O₂, and hydroxyl HO•.

receptor

Molecular structure in or on a cell that specifically recognizes and binds to a compound and acts as a physiological signal transducer, or mediator of, an effect.

Modified from [38].

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 [19]

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.

[5]

regioselectivity, regioselective

Terms referring to a reaction in which one direction of bond making or breaking occurs preferentially over all other possible directions.

Note: Reactions are termed completely (100 %) regioselective if the discrimination is complete, or partially (*x* %), if the product of reaction at one site predominates over the product of reaction at other sites.

[38]

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 be used in comparison of adverse reactions to drugs, or 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. The *relative excess risk*, *R*, is given by

$$R = (R_1 - R_0)/(R_2 - R_0)$$

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.

Note: Rate is used here as in epidemiology.

After [35]

relative risk

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

Synonym: *risk ratio*

2. Ratio of the *cumulative incidence rate* in the exposed to the cumulative incidence rate in the unexposed.

Synonym: *rate ratio*

After [35]

relative systemic availability

Quantity of metabolizable substance divided by product of quantity of absorbed substance and *exposure*.

renal

Pertaining to the kidney(s).

renal plasma flow

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

reservoir (in biology)

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

residence time

See *mean residence time*.

residual risk

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

residual time

See *mean residence time*.

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).

[1]

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 [20]

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 [20]

risk

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

[37]

2. Expected frequency of occurrence of a harmful event arising from such an exposure.

After [20]

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*.

Note: Quantification ideally requires the establishment of *dose–effect* and *dose–response* relationships in likely *target* individuals and populations.

[20]

safety factor, SF

See *uncertainty factor*

sample (in statistics)

1. Group of individuals often taken at random from a population for research purposes.

[20]

2. One or more items taken from a population or a process and intended to provide information on the population or process.

[20]

3. Portion of material selected from a larger quantity so as to be representative of the whole.

[20,24]

sampling error

That part of the total error (the estimate from a *sample* minus the population value) associated with using only a fraction of the population and extrapolating to the whole, as distinct from analytical or test error.

Note: Sampling error arises from a lack of homogeneity in the parent population.

[38]

saturable elimination

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

Scatchard plot

Method for analyzing data for freely reversible ligand/*receptor* binding interactions. The graphical plot is [bound ligand]/[free ligand] against [bound ligand], with slope the negative of the reciprocal of the binding affinity and intercept on the *x*-axis the number of receptors.

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 [57]

serum

1. Watery proteinaceous portion of the blood that remains after clotting.

Synonym: *blood serum*

2. Clear watery fluid especially that moistening the surface of serous membranes or that exuded through inflammation of any of these membranes.

[20]

short-term exposure limit, STEL

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

[2]

speciation (in chemistry)

Distribution of an element amongst defined *chemical species* in a system.

[52]

speciation analysis (in chemistry)

Analytical activities of identifying and/or measuring the quantities of one or more individual *chemical species* in a *sample*.

[52]

steady state (in chemistry)

State of a system in which properties do not change with time.

[40]

steady state (in toxicology)

State of a system in which the conditions do not change in time.

After [40]

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.

[41]

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 [65]

stochastic effect, stochastic process

Phenomenon pertaining to or arising from chance, and hence obeying the laws of probability.

After [20]

structure–activity relationship, SAR

Association between specific aspects of molecular structure and defined biological action.

[20]

See also *quantitative structure–activity relationship*.

structure-metabolism relationship, SMR

Association between the physicochemical and/or the structural properties of a substance and its metabolic behavior.

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.

[20]

subchronic effect

Biological change resulting from an environmental alteration lasting about 10 % of the lifetime of the test organism.

Note: 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.

[20]

subchronic toxicity test

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

[61]

susceptible

Describing a group of organisms more vulnerable to a given *exposure* than the majority of the population to which they belong.

Note: Susceptibility may reflect gender, age, physiological status, or genetic constitution of the organisms at risk.

synergism (in toxicology)

Pharmacological or toxicological 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 *toxicity* of each of the individual substances.

[20,38]

synergistic effect

See *synergism*.

systemic

Relating to the body as a whole.

After [20]

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.

Note: A systemic effect requires *absorption* and distribution of the substance in the body.

[20]

target (in biology)

Any organism, organ, tissue, cell, or cell constituent that is subject to the action of an agent.

After [61]

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 [20]

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*.

[2]

threshold limit value–time-weighted average, TLV–TWA

Time-weighted average *concentration* for a conventional 8-h workday and a 40-h workweek, to which it is believed nearly all workers may be repeatedly exposed, day after day, without *adverse effect*.

[2]

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.

Note: 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.

[2]

tissue/plasma partition coefficient

See *partition 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*.

Note: *Acceptable daily intake* (ADI) is normally used for substances not known to be harmful, such as food additives.

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 (in medicine)

Applied directly to the surface of the body.

topical effect

Consequence of application of a substance to the surface of the body which occurs at the point of application.

toxic

Able to cause injury to living organisms as a result of physicochemical interaction.

toxicant

See *toxic substance*.

toxicity

1. Capacity to cause injury to a living organism defined with reference to the quantity of substance administered or absorbed, the way in which the substance is administered and distributed in time (single or repeated *doses*), the type and severity of injury, the time needed to produce the injury, the nature of the organism(s) affected, and other relevant conditions.
2. *Adverse effects* of a substance on a living organism defined as in 1.
3. Measure of incompatibility of a substance with life: this quantity may be expressed as the reciprocal of the absolute value of *median lethal dose* ($1/LD_{50}$) or *concentration* ($1/LC_{50}$).

[20,38]

toxicity equivalency factor, TEF, f

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).
[20]

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 *n* components B, C ... 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:

$$n(\text{TEQ}) = \sum_{i=B}^N f_i n_i$$

After [20]

toxic substance

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

toxicity test

Experimental study of the *adverse effects* of *exposure* of a living organism to a substance for a defined duration under defined conditions.
[20]

toxicodynamics

Process of interaction of potentially *toxic substances* with *target* sites, and the biochemical and physiological consequences leading to *adverse effects*.
[20,38]

toxicogenetics

Study of the influence of hereditary factors on the effects of potentially *toxic substances* on individual organisms.
[20]

toxicokinetics

Process of the *uptake* of potentially *toxic substances* by the body, the *biotransformation* 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.
[20,38,61]

toxicologically based pharmacokinetic modeling, TBPk

See *physiologically based pharmacokinetic modeling*.

toxicology

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.
[20,38]

toxin

Poisonous substance produced by a biological organism such as a microbe, animal, or plant.
[20,38]

tracer substance

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

transcriptomics

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

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 *cell line, transformed cell*.

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 *compartmental modeling, multicompartment analysis*.

ultrafine particles

Particles in air of *aerodynamic diameters* < 0.1 μm (abbreviated to $\text{PM}_{0.1}$)

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 *tolerable daily intake* (TDI).

Note: The NOEL or NOAEL is divided by the value of the UF to calculate the ADI or TDI.

After [20]

See *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 $1 \mu\text{g l}^{-1}$ in water, or $1 \mu\text{g m}^{-3}$ in air.

Note: The excess interpretation of unit *risk* would be as follows: if unit risk = $1.5 \times 10^{-6} \mu\text{g l}^{-1}$, 1.5 excess tumors are expected to develop per 10^6 people if exposed daily for a lifetime to $1 \mu\text{g}$ of the chemical in 1 litre of drinking water.

[29]

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.

[20]

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.

[20]

xenobiotic

Compound with a chemical structure foreign to a given organism.

Note: The term is frequently restricted to manmade compounds.

After [20,38,42]

zero-order kinetics

Kinetics of a reaction in which the *rate* is independent of the *concentration*(s) of the reactants.

Synonym: *zero-order reaction*

ANNEX 1: ABBREVIATIONS AND ACRONYMS USED IN TOXICOKINETICS

ADI	acceptable daily intake
AF	assessment factor
ALARA(P)	as low as reasonably achievable (practicable) in UK, regulations relating to worker exposure in USA, goal of risk management (USNRC regulations)
AUC	area under the concentration-time curve
AUMC	area under the moment curve
BCF	bioconcentration factor
BEI	biological exposure indices (ACGIH)
BEM	biological effect monitoring
BOD	biochemical oxygen demand
b.w.	body weight
CMR	carcinogenic, mutagenic, and reproductive (toxicant)
CoMFA	comparative molecular field analysis
Cyt	cytochrome
CV	ceiling value
DNA	deoxyribonucleic acid
DNEL	derived no-effect level
EC	enzyme classification number or effective concentration
EC _n	median effective concentration to <i>n</i> % of a population
EDI	estimated daily intake
ED _n	median effective dose to <i>n</i> % 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
K_M	Michaelis constant
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol–water partition coefficient
LADD	lifetime average daily dose
LC_n	median concentration lethal to n % of a test population
LC_{50}	see LC_n
LD_n	median dose lethal to n % of a test population
LD_{50}	see LD_n
LEL	lowest-effect level, same as LOEL
LOEL	lowest-observed-effect level
LOAEL	lowest-observed-adverse-effect level
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
PBT	persistent, bioaccumulative, and toxic
PEL	permissible exposure limit
PBPK	physiologically based pharmacokinetics modeling
$PM_{2.5}$	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 modeling
TCDD	2,3,7,8-tetrachlorodibenzo[1,4]dioxin (2,3,7,8-tetrachlorooxanthrene)
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
vPvB	very persistent and very bioaccumulative

ANNEX 2: ABBREVIATIONS AND ACRONYMS OF NAMES 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 (UK)
COSHH	Control of Substances Hazardous to Health Regulations (UK)
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 (since 1998, International Council of Science)
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	Royal Society of Chemistry
REACH	Registration, Evaluation, and Authorization of Chemicals (EC)
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: SOURCES

Note: This Annex lists all the publications quoted in the text of the glossary and also all the publications consulted in order to assess current usage and nuancing of terms defined.

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