

**IUPAC GLOSSARY OF TERMS USED IN TOXICOLOGY - EXPANDED AND
REVISED FROM “GLOSSARY FOR CHEMISTS OF TERMS USED IN
TOXICOLOGY”, 1993 [1]**

(IUPAC RECOMMENDATIONS)

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Abstract

This glossary, a revision of the IUPAC “Glossary for Chemists of Terms Used in Toxicology”[1] incorporating new and redefined terms from the “Glossary of Terms Used in Toxicokinetics” [2], contains definitions and explanatory notes, if needed, for terms frequently used in the multidisciplinary field of toxicology. The glossary is compiled primarily for those scientists and others who now find themselves working in toxicology or requiring a knowledge of the subject, especially for hazard and risk assessment. Many medical terms are included because of their frequent occurrence in the toxicological literature. There are three annexes, one containing a list of abbreviations and acronyms used in toxicology, one containing a list of abbreviations and acronyms used by international bodies and by legislation relevant to toxicology and chemical safety, and one describing the classification of carcinogenicity according to the weight of evidence available.

Note: Terms for which no primary source is given have been taken verbatim from the original IUPAC “Glossary for Chemists of Terms Used in Toxicology”[1] or have been newly defined by the compilers of this paper. New or redefined terms in the “Glossary of Terms Used in Toxicokinetics” are currently referenced as in that glossary [2]. Other terms which are quoted verbatim from their sources are referenced individually. For other chemical terminology, the reader is referred to the *International Union of Pure and Applied Chemistry Compendium of Chemical Terminology* [3,4].

abiological

See synonym *abiotic*

abiotic

Not associated with living organisms.

Synonym *abiological*

abiotic degradation

Process in which a substance is converted to simpler products by physical or chemical mechanisms: examples include *hydrolysis* and *photolysis*.

abiotic transformation

Process in which a substance in the environment is modified by non-biological mechanisms.

abortifacient

Substance which induces abortion or miscarriage.

absolute lethal concentration, (LC₁₀₀)

Lowest *concentration* of a substance in an environmental medium which kills 100% of test organisms or species under defined conditions.

Note: This value is dependent on the number of organisms used in its assessment.

absolute lethal dose, (LD₁₀₀)

Lowest amount of a substance which kills 100 % of test animals under defined conditions.

Note: This value is dependent on the number of organisms used in its assessment.

absorbed dose (of a substance)

Amount (of a substance) taken up by an organism or into organs or tissues of interest.

See *absorption, systemic*

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.

absorptance (in chemistry)

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

[2]

absorption (general)

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

Note: The process may be the physical solution of a gas, liquid, or solid in a liquid, attachment of molecules of a gas, vapour, 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.

[2]

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.

Note: In mammals *absorption* is usually through the respiratory tract, gastro-intestinal tract, or skin.

[2]

absorption (of radiation)

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

[2]

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*.

[2]

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 amount to the amount of the substance (usually particles) deposited (adsorbed) in the lungs.

Synonym *absorption factor*

absorption factor

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

abuse (of drugs, substances, solvents etc.)

Improper use of drugs or other substances.

acaricide

Substance intended to kill mites, ticks or other Acaridae.

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.

[2]

acceptable daily intake (ADI) not allocated

See synonym *no acceptable daily intake allocated*

acceptable residue level of an antibiotic

Acceptable *concentration* of a residue which has been established for an antibiotic found in human or animal foods.

acceptable risk

Probability of suffering disease or injury which is considered to be sufficiently small to be "negligible".

accepted risk

Probability of suffering disease or injury which is accepted by an individual.

accidental exposure

Unintended contact with a substance or change in the physical environment (including for example radiation) resulting from an accident.

acclimatization (biological)

1. Processes, including selection and adaptation, by which a population of micro-organisms develops the ability to degrade a substance, or develops a tolerance to it.
2. In animal tests - allowing an animal to adjust to its environment prior to undertaking a study.

accumulation (in biology)

See *bioaccumulation*

accuracy

Quantity referring to the differences between the mean of a set of results or an individual result and the value which is accepted as the true or correct value for the quantity measured.

acidosis

Pathological condition in which the hydrogen ion substance concentration of body fluids is above normal and hence the pH of blood falls below the reference interval.

Antonym *alkalosis*

action level

1. *Concentration* of a substance in air, soil, water or other defined medium at which specified emergency counter-measures, such as the seizure and destruction of

contaminated materials, evacuation of the local population or closing down the sources of pollution, are to be taken.

2. Concentration of a pollutant in air, soil, water or other defined medium at which some kind of preventive action (not necessarily of an emergency nature) is to be taken.

activation (abiotic)

Conversion of a xenobiotic to a more toxic derivative by modification not involving biological catalysis.

activation (in biology)

See *bio-activation*

active ingredient

Component of a mixture responsible for the biological effects of the mixture.

Compare *inert ingredient*

active metabolite

Metabolite with biological and (or) toxicological activity.

[2]

See *metabolite*

active transport

Movement of a substance across a cell membrane against an electrochemical gradient, in the direction opposite to normal diffusion and requiring the expenditure of energy.

acute

1. Of short duration, in relation to *exposure* or effect; the effect usually shows a rapid onset.

Note: In regulatory *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 [2]

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.

Note: acute effects may occur continuously following continuous dosing or repeatedly following repeated dosing.

After [2]

acute exposure

Exposure of short duration.

[2]

See *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*.

[2]

Antonym *chronic toxicity***adaptation**

1. Change in an organism, in response to changing conditions of the environment (specifically chemical), which takes place without any irreversible disruptions of the given biological system and without exceeding normal (homeostatic) capacities of its response.
2. Process by which an organism stabilizes its physiological condition after an environmental change.

added risk

Difference between the *incidence* of an *adverse effect* in a treated group (of organisms or a group of *exposed* humans) and a control group (of the same organisms or the spontaneous incidence in humans).

addiction

Surrender and devotion to the regular use of a medicinal or pleasurable substance for the sake of relief, comfort, stimulation, or exhilaration which it affords; often with craving when the drug is absent.

additive effect

Consequence which follows *exposure* to two or more physico-chemical 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.

[2]

adduct

New chemical species AB, each molecular entity of which is formed by direct combination of two separate molecular entities A and B in such a way that there is no change in connectivity of atoms within their moieties A and B.

Note 1. Stoichiometries other than 1:1 are also possible.

Note 2. An intramolecular adduct can be formed when A and B are groups contained within the same molecular entity.

adenocarcinoma

Malignant tumour originating in glandular *epithelium* or forming recognizable glandular structures.

adenoma

Benign tumour occurring in glandular *epithelium* or forming recognizable glandular structures.

adjuvant

1. In pharmacology, a substance added to a *drug* to speed or increase the action of the main component.
2. In immunology, a substance (such as aluminium hydroxide) or an organism (such as bovine tuberculosis bacillus) which increases the response to an *antigen*.

administration (of a substance)

Application of a known amount of a substance to an organism in a reproducible manner and by a defined route.

adrenergic

See synonym *sympathomimetic*

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.

[2]

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*.

[2]

adstringent

See *astringent*

advection (in environmental chemistry)

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

[2]

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.

[2]

adverse event

Occurrence which causes an *adverse effect*.

aerobe

Organism which needs molecular oxygen for respiration and hence for growth and life.

aerobic

Requiring molecular oxygen.

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.

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.

[2]

aetiology

1. Science dealing with the cause or origin of disease.
2. In individuals, the cause or origin of disease.

after-effect of a poison

Ability of a *poison* to produce a change in an organism after cessation of contact.

age sensitivity

Quantitative and qualitative age dependence of an effect.

agonist

Substance which binds to cell *receptors* normally responding to naturally occurring substances and which produces a response of its own.

Antonym *antagonist*

air pollution

Presence of substances in the atmosphere resulting either from human activity or natural processes, in sufficient concentration, for a sufficient time and under circumstances such as to interfere with comfort, *health* or welfare of persons or to harm the environment.

air pollution control system

1. Network of organizations which monitor air pollution.
2. Group of measures or processes used to minimize or prevent air pollution.

albuminuria

Presence of albumin, derived from *plasma*, in the urine.

algicide

Substance intended to kill algae.

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.

[2]

alkalosis

Pathological condition in which the hydrogen ion substance concentration of body fluids is below normal and hence the pH of blood rises above the reference interval.

antonym *acidosis*

alkylating agent

Substance which introduces an alkyl substituent into a compound.

allele

One of several alternate forms of a *gene* which occur at the same relative position (locus) on homologous *chromosomes* and which become separated during *meiosis* and can be recombined following fusion of *gametes*.

allergen

Antigenic substance capable of producing immediate *hypersensitivity*.

allergy

Symptoms or signs occurring in sensitized individuals following exposure to a previously encountered substance (*allergen*) which would otherwise not cause such *symptoms* or *signs* in non-sensitized individuals. The most common forms of allergy are *rhinitis*, *urticaria*, *asthma*, and *contact dermatitis*.

allometric

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

[2]

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.

[2]

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.

[2]

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.

[2]

allomone

Semiochemical that is produced by an organism inducing a response in an organism of another species that is favourable to the emitter.

See *kairomone*, *synomone*

all-or-none effect

See synonym *quantal effect*

alopecia

Baldness; absence or thinning of hair from areas of skin where it is usually present.

alveol/us (pulmonary), **-i** pl., **-ar** adj.

Terminal air sac of the lung where gas exchange occurs.

ambient

Surrounding (applied to environmental media such as air, water, sediment or soil).

ambient monitoring

Continuous or repeated measurement of agents in the environment to evaluate ambient exposure and *health* risk by comparison with appropriate reference values based on knowledge of the probable relationship between exposure and resultant adverse health effects.

ambient standard

See synonym *environmental quality standard*

Ames test

In vitro test for *mutagenicity* using mutant strains of the bacterium *Salmonella typhimurium* which cannot grow in a given histidine-deficient medium: *mutagens* can

cause reverse *mutations* which enable the bacterium to grow on the medium. The test can be carried out in the presence of a given microsomal fraction (S-9) from rat liver (see *microsome*) to allow metabolic transformation of mutagen precursors to active derivatives.

amnesic shellfish poisoning, ASP

Serious illness which is a consequence of consumption of bivalve shellfish (mollusks) such as mussels, oysters and clams that have ingested, by filter feeding, large quantities of micro-algae containing domoic acid; acute symptoms include vomiting, diarrhea, and in some cases, confusion, loss of memory, disorientation and even coma.

amplification (of genes)

See synonymous term *gene amplification*

anabolism

Biochemical processes by which smaller molecules are joined to make larger molecules.
antonym *catabolism*

anaemia

Condition in which there is a reduction in the number of red blood cells or amount of haemoglobin per unit volume of blood below the reference interval for a similar individual of the species under consideration, often causing pallor and fatigue.

anaerobe

Organism which does not need molecular oxygen for life. Obligate (strict) anaerobes grow only in the absence of oxygen. Facultative anaerobes can grow either in the presence or in the absence of molecular oxygen.
antonym *aerobe*

anaerobic

Not requiring molecular oxygen.

anaesthetic

Substance which produces loss of feeling or sensation: general anaesthetic produces loss of consciousness; local or regional anaesthetic renders a specific area insensible to pain.

analgesic

Substance which relieves pain, without causing loss of consciousness.

analogue metabolism

Process by which a normally non-biodegradable compound is biodegraded in the presence of a structurally similar compound which can induce the necessary enzymes.

analytic study (in epidemiology)

Study designed to examine associations, commonly putative or hypothesized causal relationships.

anaphylaxis

Severe allergic reaction (see *allergy*) occurring in a person or animal *exposed* to an *antigen* or *haptén* to which they have previously been sensitized.

anaplasia

Loss of normal cell differentiation, a feature characteristic of most *malignancies*.

anemia

See preferred spelling *anaemia*.

aneuploid

Cell or organism with missing or extra *chromosomes* or parts of chromosomes.

anoxia

Strictly total absence of oxygen but sometimes used to mean decreased oxygen supply in tissues.

antagonism (in toxicology)

Combined effect of two or more factors which is smaller than the solitary effect of any one of those factors.

Note: 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.

antagonist (in toxicology)

Substance which decreases or eliminates the effect of another substance.

anthelmint(h)ic

Substance intended to kill parasitic intestinal worms, such as helminths.

Synonym *antihelminth*

anthracosis (coal miners' pneumoconiosis)

Form of *pneumoconiosis* caused by accumulation of carbon deposits in the lungs due to inhalation of smoke or coal dust.

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.

[2]

anti-adrenergic

See synonym *sympatholytic*

antibiotic

Substance produced by, and obtained from, certain living cells (especially bacteria, yeasts)

and moulds), or an equivalent synthetic substance, which is *biostatic* or *biocidal* at low concentrations to some other form of life, especially pathogenic or noxious organisms.

antibody

Protein (*immunoglobulin*) produced by the immune system in response to exposure to an antigenic molecule and characterized by its specific binding to a site on that molecule (antigenic determinant or *epitope*).

[4]

anticholinergic

1. adj., Preventing transmission of parasympathetic nerve impulses.
2. n., Substance which prevents transmission of parasympathetic nerve impulses.

anticholinesterase

See synonym *cholinesterase inhibitor*

anticoagulant

Substance which prevents clotting.

antidote

Substance capable of specifically counteracting or reducing the effect of a potentially *toxic* substance in an organism by a relatively specific chemical or pharmacological action.

antigen

Substance or a structural part of a substance which causes the immune system to produce specific *antibody* or specific cells and which combines with specific binding sites (*epitopes*) on the antibody or cells.

antihistamine

Substance that blocks or counteracts the action of histamine.

antihelminth

See synonym *anthelmint(h)ic*

antimetabolite

Substance, structurally similar to a *metabolite*, which competes with it or replaces it, and so prevents or reduces its normal utilization.

antimycotic

Substance used to kill a fungus or to inhibit its growth.

Synonym *fungicide*

antipyretic

Substance which relieves or reduces fever.

antiresistant

Substance used as an additive to a *pesticide* formulation in order to reduce the resistance of insects to the pesticide.

antiserum

Serum containing *antibodies* to a particular *antigen* either because of immunization or after an infectious disease.

aphasia

Loss or impairment of the power of speech or writing, or of the ability to understand written or spoken language or signs, due to a brain injury or disease.

aphicide

Substance intended to kill aphids.

aphid

Common name for a harmful plant parasite in the family Aphididae, some species of which are vectors of plant virus diseases.

aplasia

Lack of development of an organ or tissue, or of the cellular products from an organ or tissue.

apoptosis

Active process of programmed cell death requiring metabolic energy, often characterized by fragmentation of *DNA*, and without associated inflammation.

[2]

See *necrosis*

arboricide

Substance intended to kill trees and shrubs.

area source

Widespread origin of *emissions*.

area under the concentration-time curve

See *area under the curve*

area under the curve, AUC

Area between a curve and the abscissa (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.

[2]

area under the moment curve, AUMC

Area between a curve and the abscissa (horizontal axis) in a plot of (*concentration x time*) versus time.

[2]

argyria

Pathological condition characterized by grey-bluish or black pigmentation of tissues (such as skin, retina, mucous membranes, internal organs) caused by the accumulation of metallic silver, due to reduction of a silver compound which has entered the organism during (prolonged) administration or exposure.

Synonym *argyrosis*

argyrosis

See synonym *argyria*

arrhythmia

Any variation from the normal rhythm of the heartbeat.

artefact

Finding or product of experimental or observational techniques that is not properly associated with the system being studied.

arteriosclerosis

Hardening and thickening of the walls of the arteries.

arthralgia

Pain in a joint.

arthralgia saturnia

Pain in a joint resulting from lead poisoning.

arthritis

Inflammation of a joint, usually accompanied by pain and often by changes in structure.

arthrosis

1. Joint or articulation.
2. Disease of a joint.

Synonym *arthropathy*

arthropathy

See synonym *arthrosis*

asbestosis

Form of *pneumoconiosis* caused by inhalation of asbestos fibres.

ascaricide

Substance intended to kill roundworms (Ascaridae).

asphyxia

Condition resulting from insufficient intake of oxygen: symptoms include breathing difficulty, impairment of senses, and, in extreme, convulsions, unconsciousness and death.

asphyxiant

Substance that blocks the transport or use of oxygen by living organisms.

assay

1. Process of quantitative or qualitative analysis of a component of a *sample*.
2. Results of a quantitative or qualitative analysis of a component of a sample.

assimilation

Uptake and incorporation of substances by a living organism.

asthenia

Weakness; lack or loss of strength.

asthma

Chronic respiratory disease characterised by bronchoconstriction, excessive mucus secretion and *oedema* of the pulmonary alveoli, resulting in difficulty in breathing out, wheezing, and cough.

astringent

1. Adj. Causing contraction, usually locally after topical application.
2. N. Substance causing cells to shrink, thus causing tissue contraction or stoppage of secretions and discharges; such substances may be applied to skin to harden and protect it.

ataxia

Unsteady or irregular manner of walking or movement caused by loss or failure of muscular co-ordination.

atherosclerosis

Pathological condition in which there is thickening, hardening, and loss of elasticity of the walls of blood vessels, characterized by a variable combination of changes of the innermost layer consisting of local accumulation of lipids, complex carbohydrates, blood and blood components, fibrous tissue and calcium deposits. In addition, the outer layer becomes thickened and there is fatty degeneration of the middle layer.

atrophy

Wasting away of the body or of an organ or tissue.

attenuation (in genetics)

Regulation of *gene* expression in bacteria by premature termination of *transcription* of a

biosynthetic *operon*.

attractant

Substance which attracts animals. Some attractants fulfil natural biological functions such as mating or predation: others may be used to attract animals for monitoring or for control.

attributable risk

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

[2]

auto-immune disease

Pathological condition resulting when an organism produces *antibodies* or specific cells which bind to constituents of its own tissues (*autoantigens*) and cause tissue injury: examples of such disease may include rheumatoid *arthritis*, *myasthenia* gravis, and scleroderma.

auto-oxidation

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

[2]

autophagosome

Membrane-bound body (secondary *lysosome*) in which parts of the cell are digested.

autopsy

Post-mortem examination of the organs and body tissue to determine cause of death or pathological condition.

Synonym *necropsy*

autosome

Any chromosome other than a sex chromosome.

[6]

auxotroph

Organism unable to synthesize an organic molecule which is required for its growth: when the compound is given to the organism with the other nutrients it requires, growth of the organism may occur.

auxotrophy

Inability of a micro-organism to synthesize a particular organic compound required for its growth.

avicide

Substance intended to kill birds.

axenic animal

See synonym *germ free animal*

azoospermia

Less than the reference value for morphology of spermatozoa.

[6]

back-mutation

Process which reverses the effect of a *mutation* which had inactivated a *gene*; thus it restores the wild phenotype.

bacterial artificial chromosome, BAC

DNA vectors into which large DNA fragments can be inserted and cloned in a bacterial host.

[7]

bactericide

Substance intended to kill bacteria.

bagassosis

Lung disease caused by the inhalation of dust from sugar-cane residues.

base pairing

Linking of the complementary pair of polynucleotide chains of nucleic acids by means of hydrogen bonds between complementary purine and pyrimidine bases, adenine with thymine or uracil, cytosine with guanine.

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.

[2]

B-cell

See synonym *B lymphocyte*

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 %.

[2]

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 %.

[2]

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.

[2]

benchmark response

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

[2]

benefit

Advantage to or improvement in condition of an individual or a population.

benign

1. Of a disease, producing no persisting harmful effects.
2. Tumour which does not invade other tissues (*metastasis*), having lost growth control but not positional control.

Antonym *malignant*

berylliosis

See synonym *beryllium disease*

beryllium disease

Serious and usually permanent lung damage resulting from chronic inhalation of beryllium.

bias

1. Deviation of results or inferences from the truth, or processes leading to such deviation.
2. Any trend in the collection, analysis, interpretation, publication, or review of data which can lead to conclusions which are systematically different from the truth.

biased sample

Any *sample* which is not a random sample.

Antonym *random sample*

bilirubin

Orange-yellow pigment, a breakdown product of haem-containing proteins (haemoglobin, myoglobin, *cytochromes*), which circulates in the blood *plasma* bound to albumin or as water soluble glucuronides, and is excreted in the bile by the liver.

bio-accessibility

Potential for a substance to come in contact with a living organism and then interact with it. This may lead to absorption.

Note: A substance trapped inside an insoluble particle is not bio-accessible although substances on the surface of the same particle are accessible and may also be *bio-available*. Bio-accessibility, like bio-availability, is a function of both chemical speciation and biological properties. Even surface-bound substances may not be accessible to organisms which require the substances to be in solution.

bio-accessible

Able to come in contact with a living organism and interact with it.

See *bio-accessibility*

bio-accumulation

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*

bio-accumulation potential

Ability of living organisms to concentrate a substance obtained either directly from the environment or indirectly through its food.

bio-activation

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

bio-assay

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

bio-availability (general)

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

[2]

Synonyms *biological availability*, *physiological availability*

bio-availability (in pharmacokinetics)

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

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

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*.

[2]

bio-available

Able to be absorbed by living organisms.

See *bio-availability*

biochemical mechanism

Reaction or series of reactions, usually enzyme-catalysed, associated with a specific physiological event in a living organism.

biochemical (biological) oxygen demand (BOD)

Substance *concentration* of oxygen taken up through the respiratory activity of micro-organisms growing on organic compounds present when incubated at a specified temperature (usually 20° C) for a fixed period (usually 5 days). It is regarded as a measure of that organic *pollution* of water which can be degraded biologically but includes the oxidation of inorganic material such as sulfide and iron(II). The empirical test used in the laboratory to determine BOD also measures the oxygen used to oxidize reduced forms of nitrogen unless their oxidation is prevented by an inhibitor such as allyl thiourea.

biocid/e n., **-al** adj.

Substance intended to kill living organisms.

bioconcentration

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

See related term *bioaccumulation*

bioconcentration factor (BCF)

Measure of the tendency for a substance in water to accumulate in organisms, especially fish.

Note 1. 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.

Note 2. This parameter is an important determinant for human intake of aquatic food by the ingestion route.

bioconjugate

See related term *conjugate*

bioconversion

See synonym *biotransformation*

biodegradation

Breakdown of a substance catalysed by enzymes in vitro or in vivo. This may be characterized for purposes of *hazard* assessment as:

1. Primary. Alteration of the chemical structure of a substance resulting in loss of a specific property of that substance.
2. Environmentally acceptable. Biodegradation to such an extent as to remove

undesirable properties of the compound. This often corresponds to primary biodegradation but it depends on the circumstances under which the products are discharged into the environment.

3. Ultimate. Complete breakdown of a compound to either fully oxidised or reduced simple molecules (such as carbon dioxide/methane, nitrate/ammonium, and water. It should be noted that the products of biodegradation can be more harmful than the substance degraded.

bio-elimination

Removal, usually from the aqueous phase, of a test substance in the presence of living organisms by biological processes supplemented by physico-chemical reactions.

bio-equivalen/ce n., -t adj.

Relationship between two preparations of the same *drug* in the same dosage form that have a similar bioavailability.

bio-inactivation

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

[2]

bioinformatics

Discipline encompassing the development and utilization of computational facilities to store, analyse and interpret biological data.

[7]

biokinetics (in toxicology)

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

[2]

biological absorption

See *absorption, biological*

biological accessibility

See *bio-accessibility*

biological acclimatization

See *acclimatization, biological*

biological assessment of exposure

See *biological monitoring*

biological availability

See *bioavailability*

biological cycle

Complete circulatory process through which a substance passes in the biosphere. It may

involve transport through the various media (air, water, soil), followed by environmental transformation, and carriage through various ecosystems.

biological effect monitoring, BEM

Continuous or repeated measurement of early biological effects of *exposure* to a substance to evaluate ambient *exposure* and *health risk* by comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and biological effects.

biological exposure indices, BEI

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

[2]

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.

[2]

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

See *biological half life*

biological indicator

Species or group of species which is representative and typical for a specific status of an ecosystem, which appears frequently enough to serve for monitoring and whose population shows a sensitive response to changes, e.g., the appearance of a toxicant in an ecosystem.

[5]

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*.

Synonym *biological assessment of exposure*

biological oxygen demand

See synonym *biochemical oxygen demand*

biological preparation

Compound derived from living organisms and their products for use in medicine or as a *pesticide* etc.

Synonym *biological, biopreparation*

biological specimen

1. Organ, tissue (including blood), secretion or excretion product taken from an organism as a *sample* reflecting the state of the whole organism.
2. Organism taken as a sample reflecting the state of a population or their environment.

biological (germ) warfare

Military operations using any organism (bacteria, virus or other disease-causing organism) or toxin found in nature, to kill, injure or incapacitate.

biomagnification

Sequence of processes in an ecosystem by which higher *concentrations* are attained in organisms at higher trophic levels (at higher levels in the food web); at its simplest, a process leading to a higher concentration of a substance in an organism than in its food. Synonym *ecological magnification*

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, behavioural or other alteration within an organism.

[2]

biomarker of effect

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

[2]

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.

[2]

biomarker of susceptibility

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

[2]

biomass

1. Total amount of biotic material, usually expressed per unit surface area or volume, in a medium such as water.
2. Material produced by the growth of micro-organisms, plants or animals.

biomineralization

Complete conversion of organic substances to inorganic derivatives by living organisms, especially micro-organisms.

biomolecule

Substance that is synthesized by and occurs naturally in living organisms.

biomonitoring

See synonym *biological monitoring*

biopesticide

Biological agent with pesticidal activity, e.g., the bacterium *Bacillus thuringiensis* when used to kill insects.

After [5]

biopsy

Excision of a small piece of living tissue for microscopic or biochemical examination; usually performed to establish a diagnosis.

biosphere

Portion of the planet earth which supports and includes life.

biostatic

Arresting the growth or multiplication of living organisms.

biota

All living organisms as a totality.

biotransformation

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

blastocyst

Mammalian embryo at the stage at which it is implanted into the wall of the uterus.

[7]

blood-brain barrier

Physiological mechanism that alters the permeability of brain capillaries, so that some substances are prevented from entering brain tissue, while other substances are allowed to enter freely.

After [2]

blood-placenta barrier

Interface between maternal and fetal blood circulations which filters out some substances which could harm the fetus: many fat soluble substances such as alcohol are not filtered out and several types of virus can also cross this barrier.

blood plasma

See *plasma* (in biology)

blood substitution

See synonym **exchange transfusion**

blood-testis barrier

Membranous barrier separating the blood from the spermatozoa of the seminiferous tubules and consisting of specific junctional complexes between Sertoli cells.

[2]

B lymphocyte

Type of *lymphocyte* which synthesizes and secretes *antibodies* in response to the presence of a foreign substance or one identified by it as foreign. The protective effect can be mediated to a certain extent by the antibody alone (contrast *T lymphocyte*).

Synonym *B cell*

body burden

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

bolus

1. Single *dose* of a substance, originally a large pill.
2. Dose of a substance administered by a single rapid intravenous injection.
3. Concentrated mass of food ready to be swallowed.

botanical pesticide

Substance with activity against pests, that is produced naturally within a plant and may act as a defence against predators.

brady-

Prefix meaning slow as in bradycardia or bradypnoea.

bradycardia

Abnormal slowness of the heartbeat.

Antonym *tachycardia*

bradypnoea

Abnormally slow breathing.

Antonym *tachypnoea*

breathing zone

Space within a radius of 0.5 m from a person's face.

British anti-Lewisite (BAL)

See synonym *2,3-dimercaptopropan-1-ol*

bronchoconstriction

Narrowing of the air passages through the bronchi of the lungs.

Antonym *bronchodilation*

bronchodilation

Expansion of the air passages through the bronchi of the lungs.

Antonym *bronchoconstriction*

bronchospasm

Intermittent violent contraction of the air passages of the lungs.

builder

Material which enhances or maintains the cleaning efficiency of a surfactant, in a detergent, principally by inactivating water hardness; complex phosphates (especially sodium tripolyphosphate, i.e. pentasodium triphosphate), sodium carbonate, and sodium silicate are the builders most commonly used.

byssinosis

Pneumoconiosis caused by inhalation of dust and associated microbial contaminants and observed in cotton, flax, and hemp workers.

bystander exposure

Liability of members of the general public to come in contact with substances arising from operations or processes carried out by other individuals in their vicinity.

cacosmia

inappropriate perception of vile odors, including coprosmia (smelling feces) and necrosmia (the smell of death).

calcification

Process in which organic tissue becomes hardened by deposition of calcium salts within its substance.

calibration material

See synonym *reference material*

cancer

Disease resulting from the development of a *malignancy*.

carboxyhaemoglobin

Compound which is formed between carbon monoxide and haemoglobin in the blood of animals and which is incapable of transporting oxygen.

carcinogen n., -ic adj.

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

See Annex 1 for a description of classification systems for carcinogens.

carcinogen/esis n., -etic adj.

Induction, by chemical, physical, or biological agents, of *malignant neoplasms*.

carcinogenicity

Process of induction of *malignant neoplasms* by chemical, physical or biological agents.

carcinogenicity test

Long term (*chronic*) test designed to detect any possible carcinogenic effect of a test substance.

carcinoma

Malignant tumour of an epithelial cell.

Synonym *epithelioma*

cardiotoxic

Chemically harmful to the cells of the heart.

carrier

1. 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.
2. Person who is heterozygous, that is carries only one allele, for a recessive character leading to disease, and hence does not display the disease phenotype but can pass it on to the next generation.

[2]

3. Gas, liquid, or solid substance (often in particulate form) used to absorb, adsorb, dilute or suspend a substance to facilitate its transfer from one medium to another.

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*.

[2]

carrier protein

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

[2]

carrier substance

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

[2]

carry-over

1. Transfer in farming and agricultural processing of a component from one system such as soil or feed to another system such as a plant, animal or human being: carry-over is expressed as the *concentration* of the component in the second system divided by its concentration in the first.
2. Process in analytical studies by which materials are carried into a reaction mixture in which they do not belong.
3. Persistence of a substance in soil, e.g., a pesticide, such that injury may occur subsequently to a new crop.

case control study

Study which starts with the identification of persons with the disease (or other outcome variable) of interest, and a suitable control (comparison, reference) group of persons without the disease. The relationship of an attribute to the disease is examined by comparing the diseased and non-diseased with regard to how frequently the attribute is present or, if quantitative, the levels of the attribute, in the two groups.

Synonyms *case comparison study, case compeer study, case history study, case referent study, retrospective study*

catabolism

1. Reactions involving the oxidation of organic substrates to provide chemically available energy (for example ATP) and to generate metabolic intermediates.
2. Generally, process of breakdown of complex molecules into simpler ones, often providing biologically available energy.

Antonym *anabolism*

catatonia

Schizophrenia marked by excessive, and sometimes violent, motor activity and excitement, or by generalised inhibition.

cathartic

See synonym *laxative*

ceiling value, CV

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

cell cycle

Regulated biochemical steps that cells go through involving DNA replication and cell division, usually depicted as a sequential cyclical series of events.

cell line

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

See also *transformed cell line*

cell-mediated hypersensitivity

State in which an individual reacts with allergic effects caused by the reaction of *antigen*-specific *T-lymphocytes* following exposure to a certain substance (*allergen*) after having been *exposed* previously to the same substance or chemical group.

cell-mediated immunity

Immune response mediated by *antigen*-specific *T-lymphocytes*.

cell proliferation

Rapid increase in cell number.

cell strain

Cells having specific properties or markers derived from a primary culture or *cell line*.

censored data

Sample observations for which the complete distribution is not known: for example, a cohort study in which some persons cannot be followed to the predetermined end of the study ("right-censored data") or environmental assay data in which some results are less than the sample detection limit ("left-censored data").

certified reference material

Reference material provided by a certifying body such as a National Standards Organization or Metrological Laboratory or by an international body which confirms its purity and analytical values by technically valid procedures and provides a certificate detailing the relevant information.

chain of custody

Sequence of responsibility for a substance from the manufacturer to the distributor, to the user, or to the person(s) ultimately responsible for *waste* disposal. This term is also used in controlled transmission of *samples* from collection to analysis, especially of samples of materials used for medico-legal or forensic purposes.

chelation therapy

Treatment with a chelating agent to enhance the *elimination* or reduce the *toxicity* of a metal ion.

chemesthesis

Sensation of feeling evoked by airborne organic chemicals, usually occurring at concentrations above their odor thresholds.

chemical aetiologic agent

See synonym *toxic substance*

chemical conversion

Change from one chemical species to another.

[2]

chemical etiologic agent

See synonym *toxic substance*

chemical oxygen demand, COD

Substance *concentration* of available oxygen (derived from a chemical oxidizing agent) required to oxidize the organic (and inorganic) matter in *waste* water.

chemical safety

Practical certainty that there will be no *exposure* of organisms to toxic amounts of any substance or group of substances: this implies attaining an acceptably low *risk* of exposure to potentially toxic substances.

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.

[2]

chemical warfare

Military operations using the toxic properties of chemical agents to kill, injure or incapacitate.

chemophobia

Irrational fear of chemicals.

chemosis

Chemically induced swelling around the eye caused by *oedema* of the conjunctiva

chemosterilizer

Substance used to sterilize mites, insects, rodents or other animals.

chloracne

Acne-like eruption caused by *exposure* to certain chlorinated organic substances such as polychlorinated biphenyls or 2,3,7,8-tetrachlorodibenzo-p-dioxin and other dioxins.

cholinomimetic

See synonym *parasympathomimetic*

cholinesterase inhibitor

Substance which inhibits the action of acetylcholinesterase (EC 3.1.1.7) and related enzymes which catalyse the hydrolysis of choline esters: such a substance causes hyperactivity in *parasympathetic* nerves.

chromatid

Either of two filaments joined at the centromere which make up a *chromosome*.

chromatin

Stainable complex of *DNA* and proteins present in the nucleus of a *eukaryotic* cell.

chromosomal aberration

Abnormality of *chromosome* number or structure.

chromosome

Self-replicating structure consisting of *DNA* complexed with various proteins and involved in the storage and transmission of genetic information; the physical structure that contains the *genes*.

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*

[2]

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,

[2]

antonym *acute effect*

Synonym *long-term effect*

chronic exposure

Continued *exposure* or 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.

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.

antonym *acute toxicity*

chronic toxicity test

Study in which organisms are observed during the greater part of the life span and in which exposure to the test agent takes place over the whole observation time or a substantial part thereof.

antonym *acute toxicity test*

Synonym *long term test*

chronotoxicology

Study of the influence of biological rhythms on the *toxicity* of substances or of the influence of a toxicant on biological rhythms.

ciguateratoxin poisoning

Serious illness caused by eating carnivorous fish such as snappers and barracuda; gastrointestinal symptoms may accompany a wide variety of neurological symptoms including *ataxia*, *vertigo*, flaccid paralysis, respiratory arrest, and reversed perception of hot and cold; the neurological symptoms may persist for many years.

circulation of substances in the environment

Movement of *xenobiotic* substances in the environment with air flow, river current, soil, water, etc.

cirrhosis

1. Liver disease defined by histological examination and characterized by increased fibrous tissue, abnormal physiological changes such as loss of functional liver cells, and increased resistance to blood flow through the liver (portal *hypertension*).
2. Interstitial *fibrosis* of an organ.

clastogen

Agent causing *chromosome* breakage and (or) consequent gain, loss or rearrangement of pieces of chromosomes.

clastogenesis

Occurrence of chromosomal breaks and (or) consequent gain, loss or rearrangement of pieces of *chromosomes*.

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.

[2]

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 that component

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*.

[2]

cleavage

Splitting of a molecule into smaller molecules.

clinical toxicology

Scientific study involving research, education, prevention and treatment of diseases caused by chemicals, drugs and toxins.

clon/e n., -al adj.

1. Population of genetically identical cells or organisms having a common ancestor.
2. To produce such a population.
3. *Recombinant DNA* molecules all carrying the same inserted sequence.

clonic

Pertaining to alternate muscular contraction and relaxation in rapid succession.

cloning vector

Small circle of DNA (*e.g.* a plasmid) or modified bacteriophage (bacterial virus) that can carry a segment of foreign DNA into an appropriate host organism (*e.g.* a bacterial, yeast or mammalian cell).

After [7]

cluster sampling

1. A method of sampling in which the population is divided into aggregates (or clusters) of items bound together in a certain manner. A *sample* of these clusters is taken at random and all the items which constitute them are included in the sample.
2. A sampling method in which each unit selected is a group of persons (all persons in a city block, a family, etc.) rather than an individual.

cocarcinogen

Chemical, physical or biological factor which intensifies the effect of a *carcinogen*.

Codex Alimentarius

Collection of internationally adopted food standards drawn up by the Codex Alimentarius Commission, the principal body implementing the joint FAO/WHO Food Standards Programme.

cohort

Component of the population born during a particular period and identified by period of birth so that its characteristics (such as causes of death and numbers still living) can be ascertained as it enters successive time and age periods. The term "cohort" has broadened to describe any designated group of persons followed or traced over a period of time, as

in the term *cohort study* (*prospective study*).

cohort analysis

Tabulation and analysis of *morbidity* or *mortality* rates in relationship to the ages of a specific group of people (cohort), identified by their birth period, and followed as they pass through different ages during part or all of their life span. In certain circumstances such as studies of migrant populations, cohort analysis may be performed according to duration of residence in a country rather than year of birth, in order to relate *health* or mortality experience to duration of *exposure*.

cohort study

Analytic method of epidemiological study in which subsets of a defined population can be identified who are, have been, or in the future may be *exposed* or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of the method is observation of a large population for a prolonged period (years), with comparison of *incidence rates* of the given disease in groups that differ in *exposure* levels.

Synonyms *concurrent study*, *follow-up study*, *incidence study*, *longitudinal study*, *prospective study*

combined effect of poisons

Simultaneous or successive effect of two or more *poisons* on the organism by the same route of *exposure*.

cometabolism

Process by which a normally non-biodegradable substance is biodegraded only in the presence of an additional carbon source.

See also *metabolism*

comparison group

See synonym *control group*

comparative genomics

Study of the relationship of genome structure and function across different biological species.

After [7]

comparative risk

See synonym *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.

[2]

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, \dots are proportionality constants; α, β, \dots are rate constants; and t is time.

[2]

compensation

Adaptation of an organism to changing conditions of the environment (especially chemical) is accompanied by the emergence of stresses in biochemical systems which exceed the limits of normal (*homeostatic*) mechanisms. Compensation is a temporary concealed pathology which later on can be manifested in the form of explicit pathological changes (decompensation).

Synonym *pseudoadaptation*

competent authority

In the context of European Communities Directive 79/831/EEC, the Sixth Amendment to the European Community's Directive 67/548/EEC relating to the Classification, Packaging and Labelling of Dangerous Substances, official government organization or group receiving and evaluating notifications of new substances.

competent bacteria

Culture of bacteria (or yeast) treated in such a way that their ability to take up *DNA* molecules without transduction or conjugation has been enhanced.

complementary DNA, cDNA

DNA generated from an expressed messenger RNA through a process known as reverse transcription.

[7]

complete mineralization

Complete breakdown of a complex organic compound to carbon dioxide, water, oxides and oxidative inorganic products such as nitrate or sulfate.

comprehensive effect of poisons

Simultaneous or successive effect made on an organism by *poisons* entering from different media, from air, from water, from food or through the skin.

computational toxicology

Application of mathematical and computer models to predict adverse effects and to better understand the mechanism(s) through which a given chemical causes harm.

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).

[2]

concentration-effect curve

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

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.

concentration-response curve

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

[2]

concentration-response relationship

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

concord/ance n., -ant adj.

Pairs or groups of individuals of identical *phenotype*.

Note: In twin studies, this is a condition in which both twins exhibit or fail to exhibit a trait under investigation.

concurrent study

See synonym *cohort study*

concurrent validity

Measurement and its criterion refer to the same point in time: an example would be a visual inspection of a wound for evidence of infection validated against bacteriological examination of a specimen taken at the same time.

confounding

1. Situation in which the effects of two processes are not distinguishable from one another: the distortion of the apparent effect of an *exposure on risk* brought about by the association of other factors which can influence the outcome.
2. Relationship between the effects of two or more causal factors as observed in a set of data, such that it is not logically possible to separate the contribution which any single causal factor has made to an effect.
3. Situation in which a measure of the effect of an exposure on risk is distorted because of

the association of *exposure* with other factor(s) which influence the outcome under study.

confounding variable

Changing factor that can cause or prevent the outcome of interest, is not an intermediate variable, and is associated with the factor under investigation.

Synonym *confounder*

congener

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

[2]

congenital

Trait, condition or disorder that exists in an organism from birth.

After [7]

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, to make it soluble in water or *compartmentalized* within the cell.

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 an enzyme.

[2]

conjunctiva

Mucous membrane which covers the eyeball and lines the under-surface of the eyelid.

conjunctivitis

Inflammation of the *conjunctiva*.

conservative assessment of risk

Assessment of *risk* which assumes the worst possible case scenario and therefore gives the highest possible value for risk: risk management decisions based on this value will maximize safety.

construct validity

Extent to which a measurement corresponds to theoretical concepts (constructs) concerning the phenomenon under study; for example, if on theoretical grounds, the phenomenon should change with age, a measurement with construct validity would reflect such a change.

contact dermatitis

Inflammatory condition of the skin resulting from dermal *exposure* to an *allergen* (sensitizer) or an irritating (corrosive, defatting) substance.

contact poison

1. Chemical which injures the target organism through physical contact and skin absorption rather than through ingestion or inhalation.

[8]

2. Pesticide (herbicide) that causes injury to only the plant tissue to which it is applied or which is not appreciably translocated within plants.

[9]

containment

Process by which possible release, discharge or spill of a *toxic* substance during normal use or after an accident is prevented by appropriate action.

contaminant

1. Minor impurity present in a substance.

2. Extraneous material inadvertently added to a *sample* prior to or during chemical or biological analysis

3. In some contexts, as in relation to gas cleaning equipment, used as a synonym for "*pollutant*", especially on a small scale.

4. Unintended component in food that may pose a *hazard* to the consumer.

content validity

Extent to which the measurement incorporates the domain of the phenomenon under study; for example, a measurement of functional *health* status should embrace activities of daily living, occupational, family, and social functioning, etc.

contraindication

Any condition which renders some particular line of treatment improper or undesirable.

control group

Selected subjects of study, identified as a rule before a study is done, which comprises humans, animals, or other species who do not have the disease, intervention, procedure or whatever is being studied, but in all other respects are as nearly identical to the test group as possible.

Synonym *comparison group*

control, matched

Control (individual or group or case) selected to be similar to a study individual or group, or case, in specific characteristics: some commonly used matching variables are age, sex, race and socio-economic status.

convection (as applied to air and water motion)

Vertical motion of air or of water, induced by the expansion of the air or of water heated by the earth's surface, or by human activity, and its resulting buoyancy.

[2]

conversion

See *chemical conversion, biotransformation*

core grade

Quality rating, based on standard evaluation criteria established by the US Office of Pesticide Programs regulatory agencies, given to toxicological studies after submission by registrants.

corrosive

Causing a surface-destructive effect on contact; in *toxicology*, this normally means causing visible destruction of the skin, eyes, or the lining of the respiratory tract or the gastro-intestinal tract.

count mean diameter

Mean of the diameters of all particles in a population.

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.

[2]

See also *mass median diameter*

crackles

See synonym *crepitations*

crepitations

Abnormal respiratory sounds heard on auscultation of the chest, produced by passage of air through passages which contain secretion or exudate or which are constricted by spasm or a thickening of their walls; also referred to as *rhonchi*.

Note: Auscultation is the process of listening for sounds within the body by ear unassisted or using a stethoscope.

Synonyms *crackles, râles*

criterion (pl. -teria)

Validated set of data used as a basis for judgement.

criterion validity

Extent to which the measurement correlates with an external criterion of the phenomenon under study.

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.

[2]

critical dose

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

[2]

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.

[2]

critical end-point

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

critical group

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

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.

[2]

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.

[2]

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.

critical study

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

Synonym *pivotal study*

cross-product ratio

See synonym *odds ratio*

cross-sectional study (of disease prevalence and associations)

Study that examines the relationship between diseases (or other *health*-related characteristics) and other variables of interest as they exist in a defined population at one particular time.

Note: Disease *prevalence* rather than *incidence* is normally recorded in a cross-sectional

study and the temporal sequence of cause and effect cannot necessarily be determined.
Synonym *disease frequency survey, prevalence study*

cumulative effect

Overall change which occurs after repeated *doses* of a substance or radiation.
[2]

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.

Synonym *incidence proportion*

cumulative incidence rate

Proportion of the *cumulative incidence* to the total population.
[2]

cumulative incidence ratio

Value obtained by dividing the *cumulative incidence rate* in the *exposed* population by the cumulative incidence rate in the unexposed population.

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*.

cumulative risk

Probability of a common harmful effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of substances that share a common chemical mechanism of toxicity.

cutaneous

Pertaining to the skin.
Synonym *dermal*

cyanogenic

Compounds able to produce cyanide.
Examples: Cyanogenic glycosides such as amygdalin in peach and apricot stones.

cyanosis

Bluish coloration, especially of the skin and mucous membranes and fingernail beds, caused by abnormally large amounts of reduced haemoglobin in the blood vessels as a result of deficient oxygenation.

cyanotoxin

Toxin produced by Cyanobacteria, sometimes called bluegreen algae.

cytochromes

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

[2]

cytochrome P-420

Inactive derivative of cytochrome P-450 found in microsomal (see *microsome*) preparations.

cytochrome P-448

Obsolete term for *cytochrome P-450* I, A1, and A2, one of the major families of the cytochromes P-450 haemoproteins.

Note: During the mono-oxygenation of certain substances, often a detoxification process, these iso-enzymes may produce intermediates which initiate *mutations*, chemical *carcinogenesis*, *immunotoxic* reactions and other forms of chemical *toxicity*.

cytochrome P-450

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

[2]

cytogenetics

Branch of genetics which correlates the structure and number of *chromosomes* as seen in isolated cells with variation in *genotype* and *phenotype*.

cytoplasm

Fundamental substance or matrix of the cell (within the *plasma* membrane) which surrounds the nucleus, endoplasmic reticulum, mitochondria and other organelles.

cytotoxic

Causing damage to cell structure or function.

death rate

Estimate of the proportion of a population which dies during a specified period. The numerator is the number of persons dying during the period; the denominator is the size of the population, usually estimated as the mid-year population. The death rate in a population is generally calculated by the formula:

10^n (Number of deaths during a specified period) / (Number of persons at *risk* of dying during the period)

Note: This rate is an estimate of the person-time death rate, the death rate per 10^n person-

years: usually $n = 3$. If the rate is low, it is also a good estimate of the *cumulative death rate*.

Synonym *crude death rate*

decipol

Unit of perceived air quality: air on mountains or the sea has a decipol = 0.01; city air with moderate air pollution has a decipol = 0.05- 0.03; acceptable indoor air quality has decipol = 1.4 (for 80% satisfaction).

decompensation

Explicit pathophysiological changes following compensation for *adverse effects*.

decontamination

Process of rendering harmless (by neutralization, *elimination*, removal etc.) a potentially *toxic* substance in the natural environment, laboratory areas, the workplace, other indoor areas, clothes, food, water, sewage etc.

defoliant

Substance used for removal of leaves by its *toxic* action on living plants.

dehydrogenase

Enzyme which catalyses oxidation of compounds by removing hydrogen.

delayed effect

Consequence occurring after a *latent period* following the end of *exposure* to a *toxic* substance or other harmful environmental factor.

Synonym *latent effect*

denaturation

1. Addition of methanol or acetone to alcohol to make it unfit for drinking.
2. Change in molecular structure of proteins so that they cannot function normally, often caused by splitting of hydrogen bonds following *exposure* to reactive substances or heat.

denitrification

Reduction of nitrates to nitrites, nitrous oxides or dinitrogen (N_2) catalysed by facultative *aerobic* soil bacteria under *anaerobic* conditions.

dental fluorosis

Variety of tooth enamel malformations due to excessive fluoride *exposure* during dental development.

deoxyribonucleic acid, DNA

Constituent of *chromosomes* which stores the hereditary information of an organism in the form of a sequence of purine and pyrimidine bases: this information relates to the synthesis of proteins and hence it is a determinant of all physical and functional activities of the cell, and consequently of the whole organism.

deoxyribonucleic acid (DNA) cloning

Replication of DNA sequences ligated into a suitable vector in an appropriate host organism.

See *deoxyribonucleic acid*

[7]

deoxyribonucleic acid (DNA) repair

Restoration of the molecular structure of DNA after it has been damaged by a chemical or physical agent: this may involve direct DNA damage reversal, base excision repair, nucleotide excision repair, mismatch repair, or double-strand break repair

deoxyribonucleic acid (DNA) sequencing

Determining the order of base pairs in a DNA molecule can be determined.

See *deoxyribonucleic acid*

After [7]

dependence

1. A psychic craving for a *drug* or other substance which may or may not be accompanied by a physical dependency.
2. Reliance on a *drug* or other substance to maintain *health*.

depilatory

Substance causing loss of hair.

deposition

1. Process by which a substance arrives at a particular organ or tissue site, for example the deposition of particles on the ciliated epithelium of the bronchial airways.
2. Process by which a substance sediments out of the atmosphere or water and settles in a certain place.

dermal

Pertaining to the skin.

Synonym **cutaneous**

dermal irritation

Skin reaction resulting from a single or multiple *exposure* to a physical or chemical entity at the same site, characterised by the presence of inflammation; it may result in cell death.

dermatitis

Inflammation of the skin: contact dermatitis is due to local *exposure* and may be caused by irritation, allergy or infection.

descriptive epidemiology

Study of the occurrence of disease or other *health*-related characteristics in populations,

including general observations concerning the relationship of disease to basic characteristics such as age, sex, race, occupation, and social class; it may also be concerned with geographic location. The major characteristics in descriptive epidemiology can be classified under the headings: individuals, time and place.

desensitization

Suppression of sensitivity of an organism to an allergen to which the organism has been *exposed* previously.

desiccant

1. Drying agent.
2. In agriculture, a substance used for drying up plants and facilitating their mechanical harvesting.

desorption

Opposite of adsorption; a decrease in the amount of adsorbed substance.

desquamation

Shedding of an outer layer of skin in scales or shreds.

deterministic

Term applied to health effects, the severity of which varies with the dose and for which a threshold is believed to exist.

deterministic effect, deterministic process

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

See also *stochastic effect*

[2]

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 *adverse effects*.

detriment

Estimated measure of the expected harm or loss associated with an adverse event, usually in a manner chosen to facilitate meaningful addition over different events. It is generally the integrated product of arbitrary values of *risk* and *hazard* and is often expressed in terms such as costs in US dollars, loss in expected years of life or loss in productivity, and is needed for numerical exercises such as cost-benefit analysis.

developmental toxicity

Adverse effects on the developing organism (including structural abnormality, altered growth, or functional deficiency or death) resulting from *exposure* prior to conception (in

either parent), during prenatal development, or postnatally up to the time of sexual maturation.

diaphoresis

Profuse perspiration.

diaphoretic

Causing profuse perspiration.

Synonym *sudorific*

diarrheal shellfish poisoning, DSP

Serious illness which is a consequence of consumption of bivalve shellfish (mollusks) such as mussels, oysters and clams that have ingested, by filter feeding, large quantities of micro-algae containing okadaic acid; gastroenteritis develops shortly after ingestion and generally lasts 1-2 days.

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.

[2]

diffusion coefficient, D

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

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

[2]

2,3-dimercaptopropan-1-ol

Metal chelator which has been used in the treatment of arsenic, antimony, gold, mercury and lead poisoning.

Synonym *British anti-Lewisite, dimercaprol*

dimercaprol

Synonym *2,3-dimercaptopropan-1-ol*

diploid

Chromosome state in which the chromosomes are present in homologous pairs.

Note: Normal human somatic (non-reproductive) cells are diploid (they have 46 chromosomes), whereas reproductive cells, with 23 chromosomes, are haploid.

discharge

See synonym *emission*

discharge (effluent, emission) standard or release limit

Maximum amount of a *pollutant* released from a given source to a specified medium

which is acceptable under specified circumstances.

discordance (genetic)

Any difference in a character between individuals due to genetic differences such as may occur in dizygotic twins, or between matched pairs in a *case cohort study*.

Antonym *concordance*

disease

Literally, dis-ease, lack of ease; pathological condition that presents a group of symptoms peculiar to it and which establishes the condition as an abnormal entity different from other normal or pathological body states.

discontinuous effect

See synonym *intermittent effect*

dispersion (in environmental chemistry)

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

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.

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

[2]

dissipation

Reduction in the amount of a *pesticide* or other compound which has been applied to plants, soil etc. (used when it is not clear whether this is by mineralization degradation, binding, or leaching).

distributed source

See synonym *area source*

distribution

1. Apportionment of a solute between two phases. The term partition or extraction may also be used in this sense where appropriate.

[2]

2. Dispersal of a substance and its derivatives throughout the natural environment or throughout an organism. [2]

3. Final location(s) of a substance within an organism after dispersal.

distribution constant

See *partition ratio*

distribution volume

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

[2]

diuresis

Excretion of urine, especially in excess.

diuretic

Agent which increases urine production.

Synonym *micturitic*

DNA adduct

See *adduct, deoxyribonucleic acid*

DNA amplification

See *gene amplification, deoxyribonucleic acid*

DNA cloning

See *deoxyribonucleic acid cloning*

DNA repair

See *deoxyribonucleic acid repair*

DNA sequencing

See *deoxyribonucleic acid sequencing*

dominant

Allele which expresses its phenotypic effect when present in either the homozygous or the heterozygous state.

After [7]

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.

[2]

dosage

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

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

[2]

dose (of a substance)

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

[2]

dose (of radiation)

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

[2]

dose-effect

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

[2]

dose-effect curve

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

dose-effect relationship

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

[2]

dose-response curve

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

[2]

dose-response relationship

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

[2]

Draize test

Evaluation of materials for their potential to cause dermal or ocular irritation and corrosion following local *exposure*; generally using the rabbit model (almost exclusively the New Zealand White) although other animal species have been used.

drug

Any substance which when absorbed into a living organism may modify one or more of its functions.

Note: The term is generally accepted for a substance taken for a therapeutic purpose, but is also commonly used for abused substances.

Synonyms *medicine, pharmaceutical*

duplicate portion sampling method (diet/food)

Study in which test persons consume their ordinary diet but, for each meal, they prepare for subsequent analysis a duplicate portion of all food as prepared, served and consumed.

Synonym *duplicate diet study*

duplicate (replicate) samples (in chemistry)

Two (or multiple) *samples* taken under the same or comparable conditions.

dysarthria

Imperfect articulation of speech due to neuromuscular damage.

dysfunction

Abnormal, impaired, or incomplete functioning of an organism, organ, tissue or cell.

dysplasia

Abnormal development of an organ or tissue identified by morphological examination.

dyspnoea

Difficult or laboured breathing.

ecogenetics

Study of the influence of hereditary factors on the effects of *xenobiotics* on individual organisms.

ecology

Branch of biology which studies the interactions between living organisms and all factors (including other organisms) in their environment: such interactions encompass environmental factors which determine the distributions of living organisms.

ecosystem

Grouping of organisms (micro-organisms, plants, animals) interacting together, with and through their physical and chemical environments, to form a functional entity.

ecotoxicologically (environmentally) relevant concentration, ERC

Concentration of a pesticide (active ingredient, formulations, and relevant metabolites) that is likely to affect a determinable ecological characteristic of an exposed system.

After [8]

ecotoxicology

Study of the *toxic* effects of chemical and physical agents on all living organisms, especially on populations and communities within defined *ecosystems*; it includes transfer pathways of these agents and their interactions with the environment.

ectohormone

See synonym *pheromone*

ectoparasiticide

Substance intended to kill parasites living on the exterior of the host.

eczema

Acute or chronic skin inflammation with *erythema*, papules, vesicles, pustules, scales,

crusts or scabs, alone or in combination, of varied *aetiology*.

edema

See synonym *oedema*

effective concentration EC

Concentration of a substance that causes a defined magnitude of *response* in a given system.

Note: EC50 is the median concentration that causes 50 % of maximal response.

effective dose ED

Dose of a substance that causes a defined magnitude of *response* in a given system.

Note: ED50 is the median dose that causes 50 % of maximal response.

effluent

Fluid, solid or gas discharged from a given source into the external environment.

element (in molecular biology)

Sequence in the promoter region of a *gene* that regulates expression of that *gene* through interaction with a trans-acting factor.

elimination (in toxicology)

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

[2]

See also *clearance*

elimination half-life or half time

Period taken for the *plasma concentration* of a substance to decrease by half.

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*.

[2]

eliminator (of a poison)

Substance that contributes to the *elimination* of a poison from an organism.

embryo

1. Stage in the developing mammal at which the characteristic organs and organ systems are being formed: for humans, this involves the stages of development from the second to the eighth week (inclusive post conception).
2. In birds, the stage of development from the fertilization of the ovum up to hatching.
3. In plants, the stage of development within the seed.

embryonic period

Period from fertilization to the end of major organogenesis.

[6]

embryotoxicity

1. Production by a substance of *toxic* effects in progeny in the first period of pregnancy between conception and the fetal stage.
2. Any *toxic* effect on the conceptus as a result of prenatal *exposure* during the embryonic stages of development: these effects may include malformations and variations, malfunctions, altered growth, prenatal death, and altered postnatal function.

embryotropic effect

Change in the *embryo* and the regulation of its development.

emesis

Vomiting.

emission

Release of a substance from a source, including discharges to the wider environment.

Synonyms *discharge, effluent, release*

emission and exposure control

Technical and administrative procedures and specifications applied for the monitoring, reduction or *elimination* of *emissions* from a source or *exposure* to a target.

emission standard

Quantitative limit on the *emission* or discharge of a substance from a source, usually expressed in terms of a time-weighted average *concentration* or a *ceiling value*.

endemic

Present in a community or among a group of people; said of a disease prevailing continually in a region.

endocon

Portion of a conjugated metabolite which is derived from a natural product (such as a sugar, amino acid or other organic acid) of the metabolising organism.

See also *exocon, phase II reaction*.

After [4]

endocrine

Pertaining to hormones or to the glands that secrete hormones directly into the bloodstream.

endocrine disrupter

Exogenous chemical that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, its progeny or (sub)populations.

[6]

endocrine modifier

See *endocrine disrupter*

endocytosis

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

[2]

See also *phagocytosis*, *pinocytosis*

endogenous

Produced within or caused by factors within an organism.

[2]

endoplasmic reticulum

Intracellular complex of membranes in which proteins and lipids, as well as molecules for export, are synthesized and in which the *biotransformation* reactions of the mono-oxygenase enzyme systems occur.

Note: May be isolated as microsomes following cell fractionation procedures.

endothelial

Pertaining to the layer of flat cells lining the inner surface of blood and lymphatic vessels, and the surface lining of serous and synovial membranes.

endothelium

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

[2]

enteritis

Intestinal inflammation.

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.

environment

Aggregate, at a given moment, of all external conditions and influences to which a system under study is subjected.

environmental damage

Adverse effects to the natural environment.

environmental exposure level, EEL

Level (*concentration* or amount or a time integral of either) of a substance to which an organism or other component of the environment is *exposed* in its natural surroundings.

environmental fate

Destiny of a chemical or biological *pollutant* after release into the natural environment.

environmental health

Human welfare and its influence by the environment, including technical and administrative measures for improving the human environment from a *health* point of view.

environmental health impact assessment

Estimate of the *adverse effects to health* or *risks* likely to follow from a proposed or expected environmental change or development.

environmental health criteria documents

Critical publications of IPCS containing reviews of methodologies and existing knowledge - expressed, if possible, in quantitative terms - of selected substances (or groups of substances) on identifiable, immediate, and long-term effects on human *health* and welfare.

environmental hygiene

Practical control measures used to improve the basic environmental conditions affecting human *health*, for example clean water supply, human and animal *waste* disposal, protection of food from biological contamination, and housing conditions, all of which are concerned with the quality of the human environment.

Synonym *environmental sanitation*

environmental impact assessment, EIA

Appraisal of the possible environmental consequences of a past, ongoing, or planned action, resulting in the production of an environmental impact statement or 'finding of no significant impact (FONSI)'.
Environmental Recommendations

environmental impact statement, EIS

Report resulting from an *environmental impact assessment*.

environmental medicine

Specialty devoted to the prevention and management of environmental injury, illness and disability, and the promotion of the health of families, and communities by ensuring that they have a healthy environment.

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*.

environmental protection

1. Actions taken to prevent or minimize *adverse effects* to the natural environment.
2. Complex of measures including monitoring of environmental *pollution*, development and practice of environmental protection principles (legal, technical, and hygienic), including *risk assessment*, *risk management* and *risk communication*.

environmental quality objective (EQO)

Overall state to be aimed for in a particular aspect of the natural environment, for example, "water in an estuary such that shellfish populations survive in good *health*".

Note: Unlike an environmental quality standard, the EQO is usually expressed in qualitative and not quantitative terms.

environmental quality standard (EQS)

Amount *concentration* or mass concentration of a substance that should not be exceeded in an environmental system, often expressed as a *time-weighted average* measurement over a defined period.

Synonym *ambient standard*

environmental sanitation

See synonym *environmental hygiene*

environmental tobacco smoke, ETS

See synonym *sidestream smoke*

environmental transformation

Chemical transformation of substances resulting from interactions in the environment.

enzootic

Present in a community or among a group of animals; said of a disease prevailing continually in a region.

enzyme

Biological catalyst: a protein or nucleic acid which controls the rate of a biochemical reaction within a cell.

enzyme induction

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

[2]

epidemiology

Study of the distribution and determinants of *health*-related states or events in specified populations and the application of this study to control of health problems.

epigastric

Pertaining to the upper-middle region of the abdomen.

epigen/esis n., **-etic** adj.

Changes in an organism brought about by alterations in the expression of genetic information without any change in the *genome* itself: the *genotype* is unaffected by such a change but the *phenotype* is altered.

epileptiform

Occurring in severe or sudden spasms, as in convulsion or epilepsy.

epithelioma

Any tumour derived from *epithelium*.

epithelium

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

[2]

epitope

Any part of a molecule that acts as an antigenic determinant: a macromolecule can contain many different epitopes each capable of stimulating production of a different specific *antibody*.

equilibrium

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

[2]

equivalent diameter (of a particle)

Diameter of a spherical particle of the same density as a particle under investigation that, relative to a given phenomenon or property, would behave in the same way as the particle under investigation.

erythema

Redness of the skin produced by congestion of the capillaries.

eschar

Slough or dry scab on an area of skin that has been burnt.

estimated daily intake, EDI

Prediction of the daily *intake* of a residue of a potentially harmful agent based on the most realistic estimation of the residue levels in food and the best available food consumption data for a specific population: residue levels are estimated taking into account known uses of the agent, the range of contaminated commodities, the proportion of a commodity treated, and the quantity of home-grown or imported commodities.

Note: The EDI is expressed in mg residue per person.

estimated environmental concentration, EEC

Predicted concentration of a substance, typically a pesticide, within an environmental *compartment* based on estimates of quantities released, discharge patterns and inherent disposition of the substance (fate and distribution) as well as the nature of the specific receiving ecosystems.

See also *expected environmental concentration*

After [8]

estimated exposure concentration (EEC)

Measured or calculated amount or mass *concentration* of a substance to which an organism is likely to be *exposed*, considering *exposure* by all sources and routes.

estimated exposure dose (EED)

Measured or calculated *dose* of a substance to which an organism is likely to be *exposed*, considering *exposure* by all sources and routes.

estimated maximum daily intake (EMDI)

Prediction of the maximum daily intake of a residue of a potentially harmful agent based on assumptions of average food consumption per person and maximum residues in the edible portion of a commodity, corrected for the reduction or increase in residues resulting from preparation, cooking, or commercial processing.

Note: The EMDI is expressed in mg residue per person.

etiology

See *aetiology*

eukaryote

Cell or organism with the genetic material packed in a membrane-surrounded structurally discrete nucleus and with well-developed cell organelles.

Note: The term includes all organisms except archaeobacteria, eubacteria and cyanobacteria (until recently classified as cyanophyta or blue-green algae).

antonym *prokaryote*

European Inventory of Existing Chemical Substances, EINECS

List of all substances supplied either singly or as components in preparations to persons in a Member State of the European Community on any occasion between 1 January 1971 and 18 September 1981.

eutrophic

Describes a body of water with a high *concentration* of nutrient salts and a high or excessive rate of biological production.

eutrophication

Adverse change in the chemical and biological status of a body of water following depletion of the oxygen content caused by decay of organic matter resulting from high primary production as a result of enhanced input of nutrients.

excess lifetime risk

Additional or excess *risk* incurred over the lifetime of an individual by *exposure* to a *toxic* substance.

excess rate

See synonym *rate difference*

exchange transfusion

Method of active artificial *elimination* of *toxicity* consisting in complete replacement of blood of the patient by donor blood.

excipient

Any more or less inert substance added to a *drug* to give suitable consistency or form to the drug.

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

[2]

See also *clearance, elimination*

excretion rate

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

[2]

exocon

Portion of a conjugated metabolite that is derived from the parent molecule.

[4]

exogenous

Resulting from causes or derived from materials external to an organism.

antonym *endogenous*

exogenous substance

See preferred synonym *xenobiotic*

exon

Coding section of a *gene* that is separated from other coding sequences of the same *gene* by intervening noncoding sequences.

See *intron*

expected environmental concentration, EEC

Calculated concentrations of a substance, typically a pesticide, in various environmental compartments based on calculations using maximum-exposure scenarios. EEC models assume a maximum number of applications per growing season at the maximum rate of application according to the application methods stated on the product label.

After [9]

experimental model ecosystem

See synonym *microcosm*

explant

Living tissue removed from its normal environment and transferred to an artificial medium for growth.

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 constant.

[2]

exposed

Subject to a factor that is under study in the environment, for instance an environmental hazard.

antonyms *non-exposed, unexposed*

exposed group (sometimes abbreviated to **exposed**) (in epidemiology)

People (or other organisms) who have been *exposed* to a supposed cause of a disease or health state of interest, or possess a characteristic that is a determinant of the health outcome of interest.

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 micro-organisms) or intensity (for physical agents).
2. Process by which a substance becomes available for *absorption* by the *target* population, organism, organ, tissue or cell, by any route.
3. For X- or gamma 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.

[2]

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.

exposure control

See *emission and exposure control*

exposure-effect curve

See *concentration-effect curve*

exposure limit

General term defining an administrative substance *concentration* or intensity of *exposure* that should not be exceeded.

exposure ratio

In a *case control study*, value obtained by dividing the rate at which persons in the case group are *exposed* to a *risk* factor (or to a protective factor) by the *rate* at which persons in the control group are exposed to the risk factor (or to the protective factor) of interest.

exposure-response relationship

See *concentration-response relationship, dose-response relationship*

exposure surface

Surface on a target where a substance, e.g., a pesticide is present. With mammals, examples of outer exposure surfaces include the exterior of an eyeball, the skin surface and a conceptual surface over the nose and open mouth. Examples of inner exposure surfaces include the gastro-intestinal tract, the respiratory tract and the urinary tract lining.

[10]

exposure test

Determination of the level, *concentration* or *uptake* of a potentially *toxic* compound and (or) its *metabolite(s)* in biological *samples* from an organism (blood, urine, hair etc.) and the interpretation of the results to estimate the absorbed dose or degree of environmental *pollution*; or the measuring of biochemical effects, usually not direct *adverse effects* of the substance, and relating them to the quantity of substance absorbed, or to its concentration in the environment.

expressed sequence tag, EST

Partial or full complementary DNA sequence which can serve as a marker for a region of the genome which encodes an expressed product.

[7]

external validity

Generalizability of the results of a particular study, beyond the limits of the population actually studied.

extracellular space

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

[2]

extracellular volume

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

[2]

extraction ratio

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

[2]

extra risk

Probability that an agent produces an observed *response*, as distinguished from the probability that the response is caused by a spontaneous event unrelated to the agent.

extraneous residue limit, ERL

Refers to a pesticide residue or contaminant arising from environmental sources (including former agricultural uses) other than the use of a pesticide or contaminant substance directly or indirectly on the commodity. It is the maximum *concentration* of a pesticide residue or contaminant that is recommended by the *Codex Alimentarius Commission* to be legally permitted or recognized as acceptable in or on food, agricultural commodity or animal feed.

Note: The mass content is expressed in milligrams of pesticide residue or contaminant per kilogram of commodity.

extrapolation

Calculation, based on quantitative observations in *exposed* test species or *in vitro* test systems, of predicted *dose-effect* and *dose-response relationships* for a substance in humans and other biota including interspecies extrapolations and extrapolation to susceptible groups of individuals.

Note: The term may also be used for qualitative information applied to species or conditions that are different from the ones in which the original investigations were carried out.

extrapyramidal movement disorders

Involuntary movements that occur as a side effect of psychiatric medications.

fecundity

1. Ability to produce offspring frequently and in large numbers.
2. In demography, the physiological ability to reproduce.
3. Ability to produce offspring within a given period of time

[6]

feromone

See synonym *pheromone*

fertility

Ability to conceive and to produce offspring: for litter-bearing species the number of offspring per litter is used as a measure of fertility.

Note: Reduced fertility is sometimes referred to as subfertility.

fertility toxicant

Produces abnormalities of male or female reproductive functions or impairs reproductive capacity.

fertilizer

Substance applied to soil or hydroponic systems for improving the root nutrition of plants with the aim of increasing crop yields and (or) controlling production.

fetal period

See *fetus*

fetotoxicity

Toxicity to the *fetus*.

fetus (often incorrectly **foetus**)

Young mammal within the uterus of the mother from the visible completion of characteristic organogenesis until birth.

Note: In humans, this period is usually defined as from the third month after fertilisation until birth (prior to this, the young mammal is referred to as an embryo).

fibrosis

Abnormal formation of fibrous tissue.

fiducial limit

Form of confidence limit given as a stated probability, for example $P = 0.95$.

Note: In toxicology the terms fiducial limits and confidence limits are generally considered to be synonymous.

first-order process

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

[2]

2. Any process changing at a constant fractional rate.

Synonym *first-order reaction*.

[2]

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.

[2]

first pass metabolism

See *first-pass effect*

fixed dose procedure

Acute *toxicity* test in which a substance is tested initially at a small number (3 or 4) predefined *doses* to identify which produces evident toxicity without lethality: the test may be repeated at one or more higher or lower defined discriminating doses to satisfy the criteria.

fluorosis

Adverse effects of fluoride, as in dental or skeletal fluorosis.

foci (singular focus)

Small groups of cells distinguishable, in appearance or histochemically, from the surrounding tissue; indicative of an early stage of a lesion that may lead to the formation of a neoplastic nodule.

foetus

See *fetus*

follow-up study

Investigation in which individuals or populations, selected on the basis of whether they have been *exposed to risk*, have received a specified preventive or therapeutic procedure, or possess a certain characteristic, are followed to assess the outcome of *exposure*, the procedure, or effect of the characteristic, for example, occurrence of disease.

Synonym *cohort study*

food additive

Any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly) in it or its byproducts becoming a component of or otherwise affecting the characteristics of such foods.

Note: The term does not include "contaminants" or substances added to food for maintaining or improving nutritional qualities.

food allergy

Hypersensitivity reaction to substances in the diet to which an individual has previously been sensitised.

food chain

Sequence of transfer of matter and energy in the form of food from organism to organism

in ascending or descending *trophic levels*.

food intolerance

Physiologically based reproducible, unpleasant (adverse) reaction to a specific food or food ingredient that is not immunologically based.

food web

Network of *food chains*.

forced diuresis

Method of stimulating diuresis based on performing hydrational therapy, sometimes with parallel introduction of diuretics, with the aim of achieving increased clearance of a *toxic* substance in urine.

foreign substance

See preferred synonym *xenobiotic*

founder effect

Changes in allelic frequencies that occur when a small group is separated from a large population and establishes a colony in a new location.

[7]

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.

[2]

frame-shift mutation

Point *mutation* involving either the deletion or insertion of one or two nucleotides in a *gene*: by the frame shift mutation, the normal reading frame used when decoding nucleotide triplets in the *gene* is altered.

fumigant

Substance that is vaporized in order to kill or repel pests.

functional genomics

Development and implementation of technologies to characterize the mechanisms through which *genes* and their products function and interact with each other and with the environment.

[7]

fungicide

Substance intended to kill fungi.

fungus preparation

Substance obtained from fungi that has an insecticidal effect reflecting the pathogenicity

of the fungi for insects.

gamete

Reproductive cell (either sperm or egg) containing a haploid set of *chromosomes*.

gametocide

Substance intended to kill *gametes*.

gastroenteritis

Inflammation of the stomach and intestine.

gastrointestinal

Pertaining or communicating with the stomach and intestine.

gavage

Administration of materials directly into the stomach by oesophageal intubation.

gene

Length of DNA that encodes a functional product, which may be a polypeptide or a ribonucleic acid.

Note: A gene is the fundamental unit of heredity

After [7]

gene amplification

Occurrence of extra copies of a *gene*; with respect to a plasmid, an increase in the number of plasmid copies per cell, which may be induced by a specific treatment.

Note: Spontaneous *gene* amplification frequently occurs in tumour cells.

gene expression

Transcriptional activation of a *gene* so that its functional product is produced.

gene therapy

Introduction of genetic material into an individual, or the modification of the individual's genetic material, in order to achieve a therapeutic or prophylactic objective.

After [6]

genetic epidemiology

Study of the correlations between phenotypic trends and genetic variation across population groups and the application of the results of such a study to control of health problems.

gene map

Map showing the positions in the genome of *genes* or other genetic markers, either relative to each other or as a physical map of absolute distances.

genetically modified organism, GMO

Bacterium, plant or animal whose *deoxyribonucleic acid* has been deliberately altered.

genetic polymorphism

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

[2]

genetic susceptibility

Predisposition to a particular disease or sensitivity to a substance due to the presence of a specific allele or combination of alleles in an individual's genome.

After [7]

genetic toxicology

Study of chemically or physically induced changes to the structure of *DNA*, including epigenetic phenomena or mutations that may or may not be heritable.

genome

Complete set of chromosomal and extrachromosomal *genes* of an organism, a cell, an organelle, or a virus, i.e. the complete *DNA* component of an organism.

Note: This includes both the *DNA* present in the chromosomes and that in subcellular organelles (e.g. mitochondria or chloroplasts). It also includes the RNA genomes of some viruses.

[2]

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.

[2]

genotoxic

Capable of causing a change to the structure of the genome.

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.

germ-free animal

Animal grown under sterile conditions in the period of postnatal development: such animals are usually obtained by Caesarean operation and kept in special sterile boxes in which there are no viable micro-organisms (sterile air, food and water are supplied).

Synonym *axenic animal*

germ-line cell

Cell with a haploid *chromosome* content.

Note: In animals, the germ-line cells are the sperm or egg (synonym *gamete*); in plants, the pollen cell or the ovum.

After [7]

germinal aplasia

Complete failure of gonad development.

glomerular

Pertaining to a tuft or cluster, as of a plexus of capillary blood vessels or nerve fibres, especially referring to the capillaries of the glomeruli of the kidney.

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.

glomerular filtration

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

[2]

glomerular filtration rate

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

[2]

“glue sniffing”

Solvent abuse using plastic cement or other solvent-based adhesives.

glycobiology

See synonym *glycomics*

glycome

Description of the complete set of carbohydrates and their functions in a living organism

glycomics

Global study of the structure and function of carbohydrates, especially oligosaccharides (short chains of sugars) in a living organism.

Synonym *glycobiology*

gnotobiont

See synonym *gnotobio*

gnotobiota

Specifically and entirely known microfauna and microflora of a specially reared laboratory animal.

gnotobiot/e n., -ic adj.

Specially reared laboratory animal whose microflora and microfauna are specifically known in their entirety.

gonadotropic

Pertaining to effects on sex glands and on the systems that regulate them.

good agricultural practice in the use of pesticides, GAP

Nationally authorised safe uses of pesticides under actual conditions necessary for effective and reliable pest control.

Note: It encompasses a range of levels of pesticide applications up to the highest authorised use, applied in a manner that leaves a residue which is the smallest amount practicable. Authorised safe uses include nationally registered or recommended uses, that take into account public and occupational *health* and environmental safety considerations. Actual conditions include any stage in the production, storage, transport, distribution, and processing of food commodities and animal feed.

good laboratory practice principles, GLP

Fundamental rules incorporated in national regulations concerned with the process of effective organization and the conditions under which laboratory studies are properly planned, performed, monitored, recorded, and reported.

good manufacturing practice principles, GMP

Fundamental rules incorporated in national regulations concerned with the process of effective organization of production and ensuring standards of defined quality at all stages of production, distribution and marketing.

Note: Minimization of *waste* and its proper disposal are part of this process.

graded effect

Consequence that can be measured on a graded scale of intensity or severity and its magnitude related directly to the *dose* or *concentration* of the substance producing it. antonym *all-or-none effect*, *quantal effect*, *stochastic effect*

graminicide

Pesticide (herbicide) used for the control of weedy grasses (*Gramineae*).

[7]

granuloma

Granular growth or *tumour*, usually of lymphoid and epithelial cells.

ground treatment of plants

Dusting or spraying of plants with *pesticides* by hand, by special machines, or by apparatus fixed to tractors or driven by them.

guideline for exposure limits

Scientifically judged quantitative value (a *concentration* or number) of an environmental constituent that ensures aesthetically pleasing air, water or food and from which no

adverse effect is expected concerning noncarcinogenic endpoints, or that gives an acceptably low estimate of lifetime *cancer risk* from those substances which are proven human *carcinogens* or carcinogens with at least limited evidence of human *carcinogenicity*.

guideline value

Quantitative measure (a *concentration* or a number) of a constituent of an environmental medium that ensures aesthetically pleasing air, water, or food and does not result in a significant *risk* to the user.

guides to air quality

Sets of atmospheric *concentrations* and *exposure* times that are associated with specific effects of varying degrees of *pollution* on man, animals, vegetation, and the environment in general.

guides to environmental quality

Sets of *concentrations*, numbers and *exposure* times that are associated with the specific effects of factors in environmental media on man, animals, vegetation, and the environment in general.

guinea-pig maximisation test

Widely used skin test for screening possible contact *allergens*: considered to be a useful method to identify likely moderate and strong *sensitizers* in humans.

Synonym *Magnusson and Kligman test*

haem

Alternative spelling of heme

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 of 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 their 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.

[2]

Synonym *half time*

half time, $t_{1/2}$

See synonym *half life*

haploid

State in which a cell contains only one set of *chromosomes*.

Synonym *monoploid*

haplotype

1. Contraction of the phrase "haploid genotype", the genetic constitution of an individual with respect to one member of a pair of allelic genes: haplotype can refer to only one locus or to an entire genome (a genome-wide haplotype would comprise half of a diploid genome, including one allele from each allelic gene pair).

2. Set of single nucleotide polymorphisms found to be statistically associated on a single chromatid.

hapten

Low-molecular-mass *species* which is not itself antigenic unless complexed with a carrier, such as a protein. Once bound, it presents an *epitope* that can cause the *sensitization* of *lymphocytes*.

After [1]

harm

Damage or *adverse effect* to a population, species, individual organism, organ, tissue or cell.

Synonym *adverse effect*

harmful occupational factor

Component of the work environment the effect of which on a worker under certain conditions leads to ill *health* or reduction of working ability.

harmful substance

Substance that, following contact with an organism can cause ill *health* or *adverse effects* either at the time of *exposure* or later in the life of the present and future generations.

Synonym *noxious substance*

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.

See also *risk*

hazard assessment

Determination of factors controlling the likely effects of a *hazard* such as the *dose-effect* and *dose-response relationships*, variations in *target* susceptibility, and mechanism of *toxicity*.

hazard communication standard

US OSHA standard requiring all employers to inform employees of the *hazard* of substances in the workplace and the steps necessary to avoid harm.

hazard evaluation

Establishment of a qualitative or quantitative relationship between *hazard* and benefit, involving the complex process of determining the significance of the identified hazard and balancing this against identifiable benefit.

Note: This may subsequently be developed into a *risk* evaluation.

hazard identification

Determination of substances of concern, their *adverse effects*, *target* populations, and conditions of *exposure*, taking into account *toxicity* data and knowledge of effects on human *health*, other organisms and their environment.

hazard quotient, HQ

Ratio of *toxicant exposure* (estimated or measured) to a reference value regarded as corresponding to a threshold of *toxicity*: if the total *hazard* quotient from all toxicants to a target exceeds unity, the combination of toxicants may produce (will produce under assumptions of additivity) an *adverse effect*.

hazardous production factor

Production factor the effect of which on a worker under certain conditions results in injury or some impairment of *health*.

Synonym *hazard at work*, *hazardous occupational factor*

health

1. State of complete physical, mental and social well-being, and not merely the absence of disease or infirmity.
2. State of dynamic balance in which an individual's or a group's capacity to cope with the circumstances of living is at an optimal level.
3. State characterized by anatomical, physiological and psychological integrity, ability to perform personally valued family, work and community roles; ability to deal with physical, biological, psychological and social stress; a feeling of wellbeing; and freedom from the *risk* of disease and untimely death.
4. In ecology, a sustainable steady state in which humans and other living organisms can coexist indefinitely.

health advisory level, HAL

In the USA, non-regulatory health-based reference level of chemical traces (usually in ppm) in drinking water at which there are no adverse health risks when ingested over various periods of time. Such levels are established for one day, 10 days, long-term and life-time exposure periods. They contain a wide margin of safety.

health-based exposure limit

Maximum *concentration* or intensity of *exposure* that can be tolerated without significant effect (based on only scientific and not economic evidence concerning exposure levels)

and associated *health* effects).

health hazard

Any factor or *exposure* that may adversely affect *health*.

health surveillance

Periodic medico-physiological examinations of *exposed* workers with the objective of protecting *health* and preventing occupationally related disease.

healthy worker effect

Epidemiological phenomenon observed initially in studies of occupational diseases: workers usually exhibit lower overall disease and death rates than the general population, due to the fact that the old, severely ill and disabled are ordinarily excluded from employment. Death rates in the general population may be inappropriate for comparison, if this effect is not taken into account.

heavy metal (erroneous term)

Term used commonly in the toxicological literature but having no generally agreed meaning, sometimes even applied to nonmetals, and therefore a source of confusion and to be avoided. The term “metal” is adequate without the qualifying adjective but may be misleading since it implies a solid material when toxicological concern is mostly for the ionic form or another chemical species.

Synonym toxic metal (also erroneous and to be avoided)

hemes (heme derivatives)

Complexes consisting of an iron ion coordinated to a *porphyrin* acting as a tetradentate ligand, and to one or two axial ligands.

[4]

hematemesis

Vomiting of blood.

hematoma

Localised accumulation of blood, usually clotted, in an organ, space, or tissue, due to a failure of the wall of a blood vessel.

hematuria

Presence of blood in the urine.

hemodialysis

Use of an artificial kidney to remove *toxic* compounds from the blood by passing it through a tube of semipermeable membrane.

Note: The tube is bathed in a dialysing solution to restore the normal chemical composition of the blood while permitting diffusion of toxic substances from the blood.

hemoglobin

Haem-containing protein in red blood cells with an important function in transporting oxygen from the lungs to body tissues.

After [7]

hemoglobinuria

Presence of free haemoglobin in the urine.

hemolysin

Substance that damages the membrane of erythrocytes causing the release of haemoglobin.

hemolysis

Release of haemoglobin from erythrocytes, and its appearance in the *plasma*.

hemoperfusion

Passing blood through a column of charcoal or adsorbent resin for the removal of *drugs* or *toxins*.

hemosiderin

Insoluble ferric hydroxide based pigment deposited in cells in conditions of iron overload.

Henderson–Hasselbach equation

Equation of the form:

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

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.

[2]

hepatic

Pertaining to the liver.

hepatotoxic

Poisonous to liver cells.

Henry's law constant

At constant temperature and pressure, the ratio of the partial pressure of a gas above a liquid to its molal solubility in the liquid and therefore a measure of its partition between the gas phase and the solute phase.

herbicide

Substance intended to kill plants.

heterozygote

Organism which has different allelic forms of a specified *gene* on each of a pair of homologous chromosomes or describing the genome of that organism.

After [7]

Hill plot

Graphical method for analysing binding of a molecule A to a macromolecule P with n binding sites. A Hill plot of $\lg[q/(1-q)]$ vs $\lg[A]$ has a slope of 1 if binding is non-co-operative and >1 for co-operative binding.

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

[2]

histamine

Amine derived from histidine by decarboxylation and released from cells in the immune system as part of an allergic reaction: it is a powerful stimulant of gastric secretion, constrictor of bronchial smooth muscle, and vasodilator.

histogenic origin

Germ cell layer of the embryo from which a given adult tissue develops.

histology

Study (usually microscopic) of the anatomy of tissues and their cellular and subcellular structure.

histopathology

Microscopic pathological study of the anatomy and cell structure of tissues in disease to reveal abnormal or adverse structural changes.

homeostasis

Normal, internal stability in an organism maintained by co-ordinated responses of the organ systems that automatically compensate for environmental changes.

homology

Degree of identity existing between the nucleotide sequences of two related but not complementary *DNA* or *RNA* molecules.

Note 1: 70 % homology means that on the average 70 out of every 100 nucleotides are identical in a given sequence.

Note 2: The same term is used in comparing the amino acid sequences of related proteins.

homozygote

Organism which has the same allelic form of a specified *gene* on each of a pair of homologous chromosomes or describing the genome of that organism.

After [7]

hormesis (adj. hormetic)

Benefit at low dose of a substance that is harmful at a higher dose.

hormone

Substance formed in one organ or part of the body and carried in the blood to another

organ or part where it selectively alters functional activity.

human ecology

Interrelationship between humans and the entire environment - physical, biological, socio-economic, and cultural, including the interrelationships between individual humans or groups of humans and other human groups or groups of other species.

human equivalent dose

Human *dose* of an agent that is believed to induce the same magnitude of a *toxic* effect that the known animal dose has induced.

human exposure threshold (of toxicological concern)

Generic value of human exposure to a substance falling within a defined structural class, below which there is expected to be no appreciable risk to health.

hydrophilic/ adj., -ity n.

Describing the character of a molecule or atomic group which has an affinity for water.

hydrophobic/ adj., -ity n.

Describing the character of a molecule or atomic group which is insoluble in water, or resistant to wetting or hydration.

hygiene

Science of *health* and its preservation.

hyper-

Prefix meaning above or excessive: when used with the suffix "-emia" refers to blood and with the suffix "-uria" refers to urine, for example "hyperbilirubinaemia".

hyperaemia

Excessive amount of blood in any part of the body.

hyperalimentation

Ingestion or administration of nutrients in excess of optimal amounts.

hyperbilirubinaemia

Excessive *concentration* of bilirubin in the blood.

hypercalcaemia

Excessive *concentration* of calcium in the blood.

hyperglycaemia

Excessive *concentration* of glucose in the blood.

hyperkalaemia

Excessive *concentration* of potassium in the blood.

hypernatraemia

Excessive *concentration* of sodium in the blood.

hyperparathyroidism

Abnormally increased parathyroid gland activity that affects, and is affected by, *plasma calcium concentration*.

hyperplasia

Abnormal multiplication or increase in the number of normal cells in a tissue or organ.

hyper-reactivity

Term used to describe the responses of (effects on) an individual to (of) an agent when they are qualitatively those expected, but quantitatively increased.

hyper-reflexia

Exaggeration of reflexes.

hypersensitivity

State in which an individual reacts with *allergic* effects following *exposure* to a certain substance (*allergen*) after having been *exposed* previously to the same substance.

hypersusceptibility

Excessive reaction following *exposure* to a given amount or *concentration* of a substance as compared with the large majority of other *exposed* subjects.

hypertension

Persistently high blood pressure in the arteries or in a circuit, for example pulmonary hypertension or hepatic portal hypertension.

hypertrophy

Excessive growth in bulk of a tissue or organ through increase in size but not in number of the constituent cells.

hypervitaminosis

Condition resulting from the ingestion of an excess of one or more vitamins.

hypo-

Prefix meaning under, deficient: when used with the suffix "-emia" refers to blood and with the suffix "-uria" refers to urine, for example "hypocalcaemia".

hypocalcaemia

Abnormally low calcium *concentration* in the blood.

hypokalaemia

Abnormally low potassium *concentration* in the blood.

hyponatraemia

Abnormally low sodium *concentration* in the blood.

hypovolaemic

Pertaining to an abnormally decreased volume of circulating fluid (*plasma*) in the body.

hypoxaemia

Deficient oxygenation of the blood.

hypoxia

1. Abnormally low oxygen content or tension.
2. Deficiency of oxygen in the inspired air, in blood or in tissues, short of anoxia.

iatrogenic

Any adverse condition resulting from medical treatment.

icterus

Excess of bile pigment in the blood and consequent deposition and retention of bile pigment in the skin and the sclera.

idiosyncrasy

Genetically based unusually high sensitivity of an organism to the effect of certain substances.

immediately-dangerous-to-life-or-health-concentration, IDLHC

According to the US NIOSH, the maximum *exposure concentration* from which one could escape within thirty minutes without any escape-impairing symptoms or any irreversible *health* effects.

immission

Environmental *concentration* of a *pollutant* resulting from a combination of *emissions* and dispersals (often synonymous with *exposure*).

immuno-assay

Ligand-binding assay that uses a specific antigen or antibody, capable of binding to the analyte, to identify and quantify substances. The antibody can be linked to a radioisotope (radioimmunoassay, RIA) or to an enzyme which catalyses an easily monitored reaction (enzyme-linked immunosorbent assay, ELISA), or to a highly fluorescent compound by which the location of an antigen can be visualized (immunofluorescence).

[4]

immune complex

Product of an antigen-antibody reaction that may also contain components of the complement system.

immune response

Selective reaction of the body to substances that are foreign to it, or that the *immune system* identifies as foreign, shown by the production of antibodies and *antibody*-bearing cells or by a cell-mediated *hypersensitivity* reaction.

immunochemistry

Study of biochemical and molecular aspects of immunology, especially the nature of *antibodies*, *antigens* and their interactions.

immunogen

See synonym *antigen*

immunoglobulin

Family of closely related glycoproteins capable of acting as antibodies and present in *plasma* and tissue fluids; *immunoglobulin E* is the source of *antibody* in many *hypersensitivity (allergic)* reactions.

immunoglobulin E-mediated hypersensitivity

State in which an individual reacts with allergic effects caused fundamentally by the reaction of *antigen*-specific *immunoglobulin E* following *exposure* to a certain substance (*allergen*) after having been *exposed* previously to the same substance.

immunopotential

Enhancement of the capacity of the *immune system* to produce an effective response.

immunosuppression

Reduction in the functional capacity of the *immune response*; may be due to:

1. Inhibition of the normal response of the immune system to an antigen.
2. Prevention, by chemical or biological means, of the production of an *antibody* to an *antigen* by inhibition of the processes of transcription, translation or formation of tertiary structure.

immunosurveillance

Mechanisms by which the *immune system* is able to recognize and destroy *malignant* cells before the formation of an overt *tumour*.

immunotoxic

Harmful to the *immune system*.

impermeable

Of a membrane, not allowing a given substance to pass through. When applied to nonbiological membranes with no qualification, the term normally refers to water.

implantation

Attachment of the fertilized ovum (blastocyst) to the endometrium and its subsequent embedding in the compact layer, occurring 6 or 7 days after fertilization of the ovum.

[6]

in silico

Phrase applied to data generated and analysed using modelling and information technology.

New definition

in vitro

Phrase applied to a study in the laboratory, usually involving isolated organ, tissue, cells or cell fractions.

New definition

in vivo

Phrase applied to a study in an intact living organism.

New definition

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 mid-point of that period.

[2]

incidence rate (epidemiology)

Measure of the frequency at which new events occur in a population.

Note: This is the value obtained by dividing the number of new events that occur in a defined period by the population at *risk* of experiencing the event during this period, sometimes expressed as person-time.

incremental unit risk estimate

For an air pollutant, this is the additional lifetime *cancer risk* occurring in a hypothetical population in which all individuals are *exposed* continuously from birth throughout their lifetimes to a *concentration* of 1 microgram per cubic metre ($\mu\text{g m}^{-3}$) of the pollutant in the air they breathe.

indirect exposure

1. *Exposure* to a substance in a medium or vehicle other than the one originally receiving the substance.
2. Exposure of people to a substance by contact with a person directly *exposed*.

individual monitor

See synonym *personal sampler*

individual protective device, IPD

Device for individual use for protection of the whole body, eyes, respiratory pathways or

skin of workers against hazardous and harmful production factors.

Synonyms *personal protective device (PPD)*, *personal protective equipment (PPE)*

individual risk

Probability that an individual person will experience an *adverse effect*.

inducer

Substance that causes induction.

induction

Increase in the rate of synthesis of an enzyme in response to the action of an inducer or environmental conditions.

Note: Often the inducer is the substrate of the induced enzyme or a structurally similar substance (*gratuitous inducer*) that is not metabolized.

induction period

Time from the onset of *exposure* to the appearance of signs of disease.

Synonym *latent period*

industrial hygiene

See *occupational hygiene*

inert chemical

Substance that is not generally reactive.

inert ingredient

Any intentionally added ingredient of a mixture which does not contribute to the desired biological effect: this definition does not include impurities and does not imply that the inert ingredient has no biological effects.

Compare *active ingredient*

infertility (in human medicine)

Inability to become pregnant within 1 year of unprotected intercourse.

[6]

infusion (in physiology)

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

[2]

ingestion

1. Process of taking food and drink into the body by mouth.
2. Process of taking in particles by a phagocytic cell.

inhalation

Act of drawing in of air, vapour or gas and any suspended *particulates* into the lung.

inherently biodegradable

Class of compounds for which there is unequivocal evidence of *biodegradation* (primary or ultimate) in any test of biodegradability.

inhibitory concentration, IC

Concentration of a substance that causes a defined inhibition of a given system.

Note: IC50 is the median concentration that causes 50 % inhibition.

inhibitory dose, ID

Dose of a substance that causes a defined inhibition of a given system.

Note: ID50 is the median dose that causes 50 % inhibition.

initiator

1. Agent that induces a change in a *chromosome* or *gene* that leads to the induction of *tumours* after a second agent, called a *promoter*, is administered to the tissue.

2. Substance that starts a chain reaction

Note: An initiator is consumed in a chain reaction, in contrast to a catalyst.

insecticide

Substance intended to kill insects.

intake

Amount of a substance that is taken into the body, regardless of whether or not it is absorbed: the total daily intake is the sum of the daily intake by an individual from food, drinking-water, and inhaled air.

integral indicator of toxic effect

Parameter (such as body weight or temperature) characterising the overall changes in the general state of the organism *exposed* to a *toxic* substance.

interactome

Large scale protein–protein interaction map.

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.

[2]

intermittent effect

Biological change that comes and goes at intervals.

Synonym *discontinuous effect*

internal dose

See preferred synonym *absorbed dose*

internal validity

Selection and comparison of index and comparison groups in such a manner that, apart from sampling error, the observed differences between these groups with respect to dependent variables under study may be attributed only to the hypothesized effect under investigation.

interpretation (of data or findings)

Evaluation of the observations from an investigation or study in order to determine their significance for human *health*, for the environment or for both.

interspecies dose conversion

Process of extrapolating from the doses of one animal species to another, for example from rodent dose to human equivalent.

interstitial fluid

Aqueous solution filling the narrow spaces between cells.

[2]

interstitial pneumonia

Chronic form of pneumonia involving increase of the interstitial tissue and decrease of the functional lung tissue.

intervention study

Epidemiological investigation designed to test a hypothesized cause-effect relationship by intentional change of a supposed causal factor in a population.

intestinal reabsorption

Absorption further down the intestinal tract of a substance or substances that have been absorbed before and subsequently excreted into the intestinal tract, usually through the bile.

intoxication

1. Poisoning: pathological process with clinical signs and symptoms caused by a substance of exogenous or *endogenous* origin.
2. Drunkenness following consumption of beverages containing ethanol or other compounds affecting the central nervous system.

intrinsic activity

Maximal stimulatory effect induced by a compound in relation to that of a given reference compound.

[2]

intrinsic clearance

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

[2]

intrinsic factor (in biochemistry)

Specific protein required for the absorption of vitamin B₁₂ and secreted by cells in the gastric glands of the stomach.

[2]

intron

Non-coding sequence within *genes* which separates the exons (coding regions).

Note: Introns are spliced out of the messenger RNA molecule created from a *gene* after transcription and prior to translation.

After [7]

in vitro

In glass, referring to a study in the laboratory usually involving isolated organ, tissue, cell, or biochemical systems.

antonym ***in vivo***

in vivo

In the living body, referring to a study performed on a living organism.

antonym ***in vitro***

ionizing radiation

Any radiation consisting of directly or indirectly ionizing particles or a mixture of both or photons with energy higher than the energy of photons of ultraviolet light or a mixture of both such particles and photons.

irreversible alteration

Change from normal structure or function that persists or progresses after cessation of *exposure* of the organism.

irritant

1. n., Substance that causes inflammation following immediate, prolonged or repeated contact with skin, mucous membrane, or other biological material.

Note: A substance capable of causing inflammation on first contact is called a primary irritant.

2. adj., Causing inflammation following immediate, prolonged or repeated contact with skin, mucous membrane or other tissues.

ischaemia

Local deficiency of blood supply and hence oxygen to an organ or tissue owing to constriction of the blood vessels or to obstruction.

isotonic

Denoting a fluid exerting the same osmotic pressure or water potential as another fluid with which it is being compared.

itai-itai disease

Illness (renal osteomalacia) observed in the Toyama prefecture of Japan, resulting from the ingestion of cadmium-contaminated rice: damage occurred to the *renal* and skeletal-articular systems, the latter being very painful ("itai" means pain in Japanese).

jaundice

Pathological condition characterized by deposition of bile pigment in the skin and mucous membranes, including the conjunctivae, resulting in yellow appearance of the patient or animal.

joint effect

Simultaneous or successive effect of factors of diverse types (chemical, physical, biological) on an organism.

kairomone

Semiochemical that is produced by one organism inducing a response in an organism of another species that is unfavourable to the emitter.

Compare *allomone*, *synomone*

kinetics (in chemistry)

Branch of chemistry concerned with measuring and studying rates of chemical reactions. [2]

kinetics (in toxicology)

See preferred synonym *toxicokinetics*

knock-down

Technique used to decrease the expression of a particular *gene* in a cell or living organism in order to define its function.

New definition

knock-in

Technique used to express a exogenous *gene* or to overexpress an endogenous *gene* in a living organism in order to define its function.

Note: In mammalian toxicology, this technique is most readily applied to the mouse.

New definition

knock-out (in biology)

Technique used to inactivate a particular *gene* in a living organism in order to define its function.

Note: In mammalian toxicology, this technique is most readily applied to the mouse.

After [7]

lachrymation

See *lacrimation*

lacrimation

Secretion and discharge of tears.

lachrymator

See *lacrimator*

lacrimator

Substance that irritates the eyes and causes the production of tears or increases the flow of tears.

larvicide

Substance intended to kill larvae.

laryngospasm

Reflex spasmodic closure of the sphincter of the *larynx*, particularly the glottic sphincter.

larynx

Main organ of voice production, the part of the respiratory tract between the pharynx and the trachea.

lassitude

Weakness; exhaustion.

latency

See synonym *latent period*

latent effect

See synonym *delayed effect*

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.

[2]

lavage

Irrigation or washing out of a hollow organ or cavity such as the stomach, intestine or the lungs.

laxative

Substance that causes evacuation of the intestinal contents.

Synonyms *cathartic, purgative*

lesion

1. Area of pathologically altered tissue.

2. Injury or wound.
3. Infected patch of skin.

lethal

Deadly; fatal; causing death.

lethal concentration, LC

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

lethal dose, LD

Amount of a substance or physical agent (e.g. radiation) that causes death when taken into the body.

lethal synthesis

Metabolic formation of a highly *toxic* compound often leading to death of affected cells.

leukaemia

Progressive, *malignant* disease of the blood-forming organs, characterized by distorted proliferation and development of leucocytes and their precursors in the bone marrow and blood.

leukopenia

Reduced *concentration* of leukocytes in the blood.

lgK_{ow}

See synonym *lgP_{ow}*

lgP_{ow}

Logarithm to the base 10 of the partition coefficient of a substance between octan-1-ol and water.

Note: This is used as an empirical measure for lipophilicity in calculating bioaccumulation, fish *toxicity*, membrane adsorption and penetration etc.

Synonym *lgK_{ow}*

library (in bio-informatics)

Collection of DNA sequences in a searchable electronic form.

New definition

library (in molecular biology)

Collection of genomic or complementary DNA sequences that have been cloned in a vector and grown in an appropriate host organism (e.g. bacteria, yeast).

After [6]

life-long exposure

Subjection to a potentially *toxic* substance during the whole lifetime.

limacide

Substance intended to kill mollusca including the gastropod mollusc, *Limax*.

limit recommended

See synonym *recommended limit*

limit test

Acute *toxicity* test in which, if no ill-effects occur at a pre-selected maximum dose, no further testing at greater *exposure* levels is required.

limit value (LV)

Limit *concentration* at or below which Member States of the European Community must set their *environmental quality standard* and *emission standard* for a particular substance according to Community Directives.

limited evidence

According to the US EPA's guidelines for Carcinogen *Risk Assessment*, "limited evidence" is a collection of facts and accepted scientific inferences that suggests that an agent may be causing an effect, but this suggestion is not strong enough to be considered established fact.

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*.

lipophilic/ adj., -ity n.

Having an affinity for fat and high lipid solubility.

Note: This is a physicochemical property which describes a partitioning equilibrium of solute molecules between water and an immiscible organic solvent, favouring the latter, and which correlates with bioaccumulation.

Synonym *hydrophobicity*

Antonym *hydrophilicity, lipophobicity*

lipophobic/ adj., -ity n.

Having a low affinity for fat and a high affinity for water.

Synonym *hydrophilicity*

Antonym *hydrophobicity, lipophilicity*

liposome

1. Artificially formed lipid droplet, small enough to form a relatively stable suspension in aqueous media, useful in membrane transport studies and in *drug* delivery.
2. Lipid droplet in the endoplasmic reticulum of a fatty liver.

After [1]

local effect

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

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 unlabelled 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.

[2]

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*.

log-normal transformation

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

[2]

long-term effect

See synonym *chronic effect*

long-term exposure

See synonym *chronic exposure*

long-term toxicity

See synonym *chronic toxicity*

lowest effective dose, LED

Lowest *dose* of a chemical inducing a specified effect in a specified fraction of *exposed* individuals.

[2]

lowest lethal concentration found

See synonym *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*.

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*.

lymphocyte

Animal cell that interacts with a foreign substance or organism, or one which it identifies as foreign, and initiates an immune response against the substance or organism.

Note: There are two main groups of lymphocytes, B lymphocytes and T lymphocytes.

lymphoma

General term comprising *tumours* and conditions allied to tumours arising from some or all of the cells of lymphoid tissue.

lysimeter

Laboratory column of selected representative soil or a protected monolith of undisturbed field soil with which it is possible to *sample* and monitor the movement of water and substances.

lysosome

Membrane-bound cytoplasmic organelle containing hydrolytic enzymes.

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.

macroscopic (gross) pathology

Study of changes associated with disease that are visible to the naked eye without the need for a microscope.

Mad Hatter syndrome

See synonym *mercurialism*

Magnusson and Kligman test

See synonym *guinea-pig maximisation test*

mainstream smoke (tobacco smoking)

Smoke that is inhaled.

malaise

Vague feeling of bodily discomfort.

malignancy

Population of cells showing both uncontrolled growth and a tendency to invade and destroy other tissues.

Note: A malignancy is life-threatening.

malignant

1. Tending to become progressively worse and to result in death if not treated.
2. In cancer, cells showing both uncontrolled growth and a tendency to invade and destroy other tissues.

antonym *benign*

mania

Emotional disorder (mental illness) characterized by an expansive and elated state (euphoria), rapid speech, flight of ideas, decreased need for sleep, distractability, grandiosity, poor judgement and increased motor activity.

margin of exposure, MOE

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

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.

mass median diameter

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

material safety data sheet, MSDS

Compilation of information required under the US OSHA *Hazard* Communication Standard on the identity of hazardous substances, *health* and physical *hazards*, *exposure* limits, and precautions.

maximum allowable (admissible, acceptable) concentration, MAC

Regulatory value defining the *concentration* that if inhaled daily (in the case of work people for 8 hours with a working week of 40 hours, in the case of the general population 24 hours) does not, in the present state of knowledge, appear capable of causing appreciable harm, however long delayed during the working life or during subsequent life or in subsequent generations.

maximum average daily concentration of an atmospheric pollutant

Highest of the average daily *concentrations* recorded at a definite point of measurement during a certain period of observation.

Synonym **peak daily average concentration of an air pollutant**

maximum contaminant level, MCL

Under the Safe Drinking Water Act (USA), primary MCL is a regulatory *concentration* for drinking water which takes into account both *adverse effects* (including sensitive populations) and technological feasibility (including natural background levels): secondary MCL is a regulatory concentration based on “welfare”, such as taste and staining, rather than *health*, but also takes into account technical feasibility. MCL Goals (MCLG) under the Safe Drinking Water Act do not consider feasibility and are zero for all human and animal *carcinogens*.

maximum exposure limit, MEL

Occupational *exposure* limit legally defined in GB under COSHH as the maximum *concentration* of an airborne substance, averaged over a reference period, to which employees may be *exposed* by inhalation under any circumstances, and set on the advice of the HSC Advisory Committee on *Toxic Substances*.

maximum permissible concentration, MPC

See synonym *maximum allowable concentration*

maximum permissible daily dose

Maximum daily dose of substance whose penetration into a human body during a lifetime will not cause diseases or *health hazards* that can be detected by current investigation methods and will not adversely affect future generations.

maximum permissible level, MPL

Level, usually a combination of time and *concentration*, beyond which any *exposure* of humans to a chemical or physical agent in their immediate environment is unsafe.

maximum residue limit for pesticide residues, MRL

Maximum contents of a *pesticide* residue (expressed as mg kg^{-1} fresh weight) recommended by the *Codex Alimentarius Commission* to be legally permitted in or on food commodities and animal feeds.

Note: MRL's are based on data obtained following *good agricultural practice* and foods derived from commodities that comply with the respective MRL's are intended to be toxicologically acceptable.

maximum residue limit for veterinary drugs, MRL

Maximum contents of a *drug* residue (expressed as mg kg^{-1} or $\mu\text{g kg}^{-1}$ fresh weight) recommended by the *Codex Alimentarius Commission* to be legally permitted or recognized as acceptable in or on food commodities and animal feeds.

Note: The MRL is based on the type and amount of residue considered to be without any toxicological *hazard* for human *health* as expressed by the acceptable daily intake (ADI) or on the basis of a temporary ADI that uses an additional uncertainty factor. It also takes into account other relevant public health *risks* as well as food technological aspects.

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).

maximum tolerable dose, MTD

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

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.

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 1: 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 2: In some studies, toxicity that could interfere with a carcinogenic effect is specifically excluded from consideration.

maximum velocity, V_{\max}

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

[2]

Synonym *maximum rate*

mean life

Average lifetime of a molecular, atomic, or nuclear system in a specified state.

Note: For an exponentially decaying system, it is the average time for the number of molecules, atoms or nuclei in a specified state to decrease by a factor of e , the base of natural logarithms.

Synonym *mean time*

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 [2]

median effective concentration, EC₅₀

Statistically derived median *concentration* of a substance in an environmental medium expected to produce a certain effect in 50% of 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.

median effective dose, ED₅₀

Statistically derived median *dose* of a chemical or physical agent (radiation) expected to produce a certain effect in 50% of 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.

median lethal concentration, LC₅₀

Statistically derived median *concentration* of a substance in an environmental medium expected to kill 50% of organisms in a given population under a defined set of conditions.

median lethal dose, LD₅₀

Statistically derived median *dose* of a chemical or physical agent (radiation) expected to kill 50% of organisms in a given population under a defined set of conditions.

median lethal time, TL₅₀

Statistically derived median 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.

median narcotic concentration, NC₅₀

Statistically derived median *concentration* of a substance in an environmental medium expected to cause *narcotic* conditions in 50 % of a given population under a defined set of conditions.

median narcotic dose, ND₅₀

Statistically derived dose of a substance expected to cause *narcotic* conditions in 50 % of test animals under a defined set of conditions.

medicine

Any drug or remedy.

Note: Any substance may be used as a drug or a remedy; the end effect will depend on the dose.

meiosis

1. Process of "reductive" cell division, occurring in the production of *gametes*, by means

of which each daughter nucleus receives half the number of *chromosomes* characteristic of the somatic cells of the species.

2. See *miosis*.

mercurialism

Chronic poisoning caused by the excessive use of mercury, by breathing its vapour, or by *exposure* in mining or smelting processes.

Synonym *Mad Hatter syndrome*

mesocosm

See *microcosm*

mesothelioma

Malignant tumour of the mesothelium of the pleura, pericardium or peritoneum, that may be caused by *exposure* to asbestos fibres and some other fibres.

metabolic activation

Biotransformation of a substance to a more biologically active derivative.

[2]

Synonym *bio-activation*

metabolic enzymes

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

[2]

metabolic half-life

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

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

Synonym *metabolic half-time*

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*.

metabolic transformation

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

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.

metabolite

Intermediate or product resulting from *metabolism*.

metabolomics

See *metabonomics*

metabonomics

Evaluation of cells, tissues or biological fluids for changes in *metabolite* levels that follow *exposure* to a given substance, in order to determine the metabolic processes involved, to evaluate the disruption in intermediary metabolic processes that results from exposure to that substance, or to determine the part of the genome that is responsible for the changes.

After [2]

metaplasia

Abnormal transformation of an adult, fully differentiated tissue of one kind into a differentiated tissue of another kind.

metastasis

1. Movement of bacteria or body cells, especially *cancer* cells, from one part of the body to another, resulting in change in location of a disease or of its symptoms from one part of the body to another.
2. Growth of pathogenic micro-organisms or of abnormal cells distant from the site of their origin in the body.

methaemoglobinaemia

Presence of methaemoglobin (oxidized haemoglobin) in the blood in greater than normal proportion.

methaemoglobin-forming substance

Substance capable of oxidising directly or indirectly the iron(II) in haemoglobin to iron(III) to form methaemoglobin, a derivative of haemoglobin that cannot transport oxygen.

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.

[2]

Michaelis-Menten kinetics

Dependence of an initial rate of reaction upon the *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 behaviour 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:

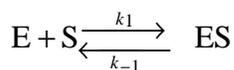
QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.

in which case $K_M = (k_{-1} + k_{cat})/k_1$ (Briggs-Haldane conditions). It has more usually been applied only to the special case in which $k_{-1} \gg k_{cat}$ 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).

[2]

Michaelis-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:

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

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.

[2]

micro-albuminuria

Chronic presence of albumin in slight excess in urine.

micro-array

Grid of nucleic acid molecules of known sequence linked to a solid substrate, which can be probed with a sample containing either messenger RNA or *complementary DNA* from a cell or tissue to reveal changes in *gene* expression relative to a control sample.

Note: Micro-array technology, which is also known as “DNA chip” technology, allows the expression of many thousands of *genes* to be assessed in a single experiment.

After [6]

microcosm

Artificial test system that simulates major characteristics of the natural environment for the purposes of ecotoxicological assessment.

Note: Such a system would commonly have a terrestrial phase, with substrate, plants and herbivores, and an aquatic phase, with vertebrates, invertebrates and plankton. The term "*mesocosm*" implies a more complex and larger system than the term "*microcosm*" but the distinction is not clearly defined.

Synonym *experimental model ecosystem*

micromercurialism

Effects of *exposure* to mercury detected at the lowest exposure levels producing a measurable reaction.

microsome

Artefactual spherical particle, not present in the living cell, derived from pieces of the endoplasmic reticulum present in homogenates of tissues or cells.

Note: microsomes sediment from such homogenates when centrifuged at 100 000 g and higher: the microsomal fraction obtained in this way is often used as a source of mono-oxygenase enzymes.

micturitic

See synonym *diuretic*

midstream sampling

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

[2]

Minamata disease

Neurological disease caused by ingestion of methylmercury-contaminated fish, first seen at Minamata Bay in Japan.

mineralization

Complete conversion of organic substances to inorganic derivatives.

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.

minimum lethal dose, LD_{min}

Lowest amount of a substance that, when introduced into the body, may cause death to individual species of test animals under a defined set of conditions.

miosis

Abnormal contraction of the pupil of the eye to less than 2 mm.
Alternative spelling (obsolete): meiosis

miscible

Liquid substances capable of mixing without separation into two phases; refers to liquid mixtures.

miticide

Substance used for the control of mites.

mitochondri/on (pl /a)

Eukaryote cytoplasmic organelle that is bounded by an outer membrane and an inner membrane; the inner membrane has folds called cristae that are the centre of ATP synthesis in oxidative phosphorylation in the animal cell and supplement ATP synthesis by the chloroplasts in photosynthetic cells.

Note: The mitochondrial matrix within the inner membrane contains ribosomes, many oxidative enzymes, and a circular *DNA* molecule that carries the genetic information for a number of these enzymes.

mitogen

Substance that induces *lymphocyte* transformation or, more generally, *mitosis* and cell proliferation.

mitosis

Process by which a cell nucleus divides into two daughter nuclei, each having the same genetic complement as the parent cell: nuclear division is usually followed by cell division.

mixed function oxidase, MFO

See synonym *mono-oxygenase*

modifying factor, MF

See *safety factor*, *uncertainty factor*

molluscicide

Substance intended to kill molluscs.

Synonym *limacide*

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*.

monoclonal

Pertaining to a specific protein from a single clone of cells, all molecules of this protein being the same.

monoclonal antibody

Antibody produced by cloned cells derived from a single *lymphocyte*.

mono-oxygenase

Enzyme that catalyses reactions between an organic compound and molecular oxygen in which one atom of the oxygen molecule is incorporated into the organic compound and one atom is reduced to water; involved in the *metabolism* of many natural and foreign compounds giving both unreactive products and products of different or increased *toxicity* from that of the parent compound.

Note: Such enzymes are the main catalysts of phase 1 reactions in the metabolism of *xenobiotics* by the endoplasmic reticulum or by preparations of *microsomes*.

Synonym *mixed function oxidase*

Monte Carlo study

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

[2]

morbidity

Any departure, subjective or objective, from a state of physiological or psychological well-being: in this sense, "sickness", "illness", and "morbid condition" are similarly defined and synonymous.

morbidity rate

Term (to be avoided) used loosely to refer to *incidence* or *prevalence* rates of disease.

morbidity survey

Method for the estimation of the *prevalence* and (or) *incidence* of a disease or diseases in a population.

mordant

Substance that fixes a dyestuff in or on a material by combining with the dye to form an insoluble compound, used to fix or intensify stains in a tissue or cell preparation.

mortality

Death as studied in a given population or subpopulation.

Note: The word mortality is often used incorrectly instead of mortality rate.

mortality rate

See synonym *death rate*

mortality study

Investigation dealing with death rates or proportion of deaths attributed to specific causes as a measure of response.

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.

[2]

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).

[2]

multicompartment model

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

[2]

multifactorial disease

Illness with pathology dependent on complex interplay of genetic and (or) environmental factors.

After [7]

multigeneration study

1. *Toxicity* test in which two to three generations of the test organism are *exposed* to the substance being assessed.
2. *Toxicity* test in which only one generation is exposed and effects on subsequent generations are assessed.

multiple chemical sensitivity

Allergic condition attributed to extreme sensitivity to various environmental chemicals, found in air, food, water, building materials, or fabrics.

multiple (or multiphasic) screening

Procedure that has evolved by combining single screening tests, and is the logical corollary of mass screening.

Note 1: Where much time and effort have been spent by a population in attending for a single test such as mass radiography, it is natural to consider the economy of offering other tests at the same time.

Note 2: Multiple (or multiphasic) screening implies the administration of a number of tests, in combination, to large groups of people.

multipotent

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

[2]

multistage cluster sampling

Cluster sampling with more than two stages, each sampling being made on aggregates (or clusters) in which the clusters already obtained by the preceding sampling have been divided.

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.

[2]

multistage sampling

Type of sampling in which the *sample* is selected by stages, the sampling units at each stage being subsampled from the larger units chosen at the previous stage.

multivariate statistics

Set of statistical tools to analyse data matrices using regression and (or) pattern recognition techniques.

[2]

murine

Of or belonging to the family of rats and mice (Muridae).

mutagen

Agent that can induce heritable changes (*mutations*) of the *genotype* in a cell as a consequence of alterations in or loss of genetic material.

mutagenesis

Introduction of heritable changes (*mutations*) of the *genotype* in a cell as a consequence of alterations or loss of *genes* or *chromosomes* (or parts thereof).

mutagenicity

Ability of a physical, chemical, or biological agent to induce heritable changes (*mutations*) in the genotype in a cell as a consequence of alterations or loss of *genes* or *chromosomes* (or parts thereof).

mutation

Any relatively stable heritable change in genetic material that may be a chemical transformation of an individual *gene* (*gene* or point *mutation*), altering its function, or a rearrangement, gain or loss of part of a *chromosome*, that may be microscopically visible (chromosomal mutation).

Note: Mutation can be either germinal, and inherited by subsequent generations, or somatic and passed through cell lineage by cell division.

myalgia

Pain or tenderness in a muscle or group of muscles.

myasthenia

Muscular weakness.

mycotoxin

Toxin produced by a fungus.

mydriasis

Extreme dilation of the pupil of the eye, either as a result of normal physiological response or in response to a chemical *exposure*.

myelosuppression

Reduction of bone marrow activity leading to a lower *concentration* of platelets, red cells and white cells in the blood.

nanoparticle

Microscopic particle whose size is measured in nanometers, often restricted to so-called nanosized particles (NSPs; < 100 nm in aerodynamic diameter), also called ultrafine particles (see separate entry).

nanotoxicology

Scientific discipline involving the study of the actual or potential danger presented by the harmful effects of nanoparticles 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.

narcotic

1. Nonspecific usage - an agent that produces insensibility or stupor.
2. Specific usage - an opioid, any natural or synthetic *drug* that has morphine-like actions.

natriuretic

Substance increasing the rate of excretion of sodium ion in the urine.

natural occurrence

Presence of a substance in nature, as distinct from presence resulting from inputs from human activities.

Note: The contamination of the natural environment by some man-made compounds may be so widespread that it is practically impossible to get access to biota with a truly natural level; only 'normal' levels can be measured, those which are usually prevalent in places where there is no obvious local contamination.

necropsy

See synonym *autopsy*

necrosis

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

[2]

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.

nematicide (nematocide)

Substance used for the control of nematodes.

neonat/e n., -al adj.

Infant during the first 4 weeks of postnatal life

Note: For statistical purposes some scientists have defined the period as the first 7 days of postnatal life.

neoplas/ia, -m

New and abnormal formation of tissue as a *tumour* or growth by cell proliferation that is faster than normal and continues after the initial stimulus (i) that initiated the proliferation has ceased.

nephritis

Inflammation of the kidney, leading to kidney failure, usually accompanied by *proteinuria, haematuria, oedema, and hypertension*.

nephrotoxic

Chemically harmful to the cells of the kidney.

neural

Pertaining to a nerve or to the nerves.

neurologic shellfish poisoning, (NSP)

Serious illness which is a consequence of consumption of toxic bivalve shellfish (mollusks) such as mussels, oysters and clams that have ingested, by filter feeding, large quantities of micro-algae containing brevetoxin; symptoms include *gastroenteritis*; rectal burning; *paresthesias* of the face, trunk, and limbs; *myalgias*; *ataxia*; *vertigo*; and reversal of hot/cold sensation.

neuron(e)

Nerve cell, the morphological and functional unit of the central and peripheral nervous systems.

neuropathy

Any disease of the central or peripheral nervous system.

neurotoxic/ adj., -ity n.

Able to produce chemically an *adverse effect* on the nervous system: such effects may be subdivided into two types.

1. Central nervous system effects (including transient effects on mood or performance and pre-senile dementia such as Alzheimer's disease).
2. Peripheral nervous system effects (such as the inhibitory effects of organophosphorus compounds on synaptic transmission).

nitrification

Sequential oxidation of ammonium salts to nitrite and nitrate by micro-organisms.

nitrosative stress

Adverse effects occurring when the generation of reactive nitrogen species in a system exceeds the system's ability to neutralize and eliminate them; nitrosative stress may lead to nitrosylation reactions that can alter protein structure thus inhibiting normal function.

no-acceptable-daily-intake-allocated

This expression is applicable to a substance for which the available information is not sufficient to establish its safety, or when the specifications for identity and purity are not adequate, or when the available data show that the substance is hazardous and should not be used.

Note: The basis for the use of the expression should be determined before action is taken; in the first two cases above, not being able to allocate an ADI does not mean that the substance is unsafe.

n-octanol-water partition coefficient

See synonym *octanol-water partition coefficient*

nodule

Small node or boss that is solid and can be detected by touch.

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).

non-bioenvironmental transformation

Change in the chemical or physical nature of a substance occurring as a result of physicochemical conditions and independent of any biological system.

no-effect-dose, NED

Amount of a substance that has no effect on the organism.

Note: It is lower than the threshold of harmful effect and is estimated while establishing the threshold of harmful effect.

Synonym *subthreshold dose*

non-occupational exposure

Environmental *exposure* outside the workplace to substances that are otherwise associated with particular work environments and (or) activities and processes that occur there.

nonstochastic

See preferred term *deterministic*.

non-target organism

Organism affected by a *pesticide* although not the intended object of its use.

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*.

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*.

no-response-level, NRL

Maximum *dose* of a substance at which no specified response is observed in a defined population and under defined conditions of *exposure*.

nosocomial

Associated with a hospital or infirmary, especially used of diseases that may result from treatment in such an institution.

noxious substance

See synonym *harmful substance*

nucleus (in cell biology)

Compartment in the interphase eukaryotic cell bounded by a double membrane and containing the genomic DNA, with the associated functions of transcription and processing.

nuisance threshold

Lowest *concentration* of an air pollutant that can be considered objectionable.

nutritional table method

Procedure for evaluating the dietary intake of a large number of people.

Note 1: The accuracy of the method depends on the accuracy with which records of the food consumption can be established and the accuracy of the nutritional tables specifying the *concentration* of various nutrients, vitamins, essential, and non-essential substances including pesticide residues.

Note 2: For each record of quantity of food consumed during a certain time period, the daily intake of the substance in question is calculated by multiplying the substance concentration in the food item (as obtained from the nutritional table) by the quantity of food consumed and dividing by the time of observation.

nystagmus

Involuntary, rapid, rhythmic movement (horizontal, vertical, rotary, mixed) of the eyeball, usually caused by a disorder of the labyrinth of the inner ear or a malfunction of the central nervous system.

objective environment

Actual physical, chemical, and social environment as described by objective measurements, such as noise levels in decibels and *concentrations* of air *pollutants*.

occupational environment

Surrounding conditions at a workplace.

occupational exposure

Experience of substances, intensities of radiation etc. or other conditions while at work.

occupational exposure limit, OEL

Regulatory level of *exposure* to substances, intensities of radiation etc. or other conditions, specified appropriately in relevant government legislation or related codes of practice.

occupational exposure standard, OES

1. Level of *exposure* to substances, intensities of radiation etc. or other conditions considered to represent specified good practice and a realistic criterion for the control of exposure by appropriate plant design, engineering controls, and, if necessary, the addition and use of personal protective clothing.

2. In GBR, *health*-based exposure limit defined under COSHH Regulations as the *concentration* of any airborne substance, averaged over a reference period, at which, according to current knowledge, there is no evidence that it is likely to be injurious to employees, if they are *exposed* by inhalation, day after day, to that concentration, and set on the advice of the HSE Advisory Committee on *Toxic Substances*.

occupational hygiene

Identification, assessment and control of physicochemical and biological factors in the workplace that may affect the *health* or well-being of those at work and in the surrounding community.

occupational medicine

Specialty devoted to the prevention and management of occupational injury, illness and disability, and the promotion of the health of workers, their families, and their communities.

occupational safety and health

See *occupational hygiene*

octanol-water partition coefficient, P_{ow} , K_{ow}

Measure of lipophilicity by determination of the equilibrium distribution between octan-1-ol and water, as used in pharmacological studies and in the assessment of environmental fate and transport of organic chemicals.

ocular

Pertaining to the eye.

odds

Ratio of the probability of occurrence of an event to that of non-occurrence, or the ratio of the probability that something is so, to the probability that it is not so.

odds ratio, OR

Quotient obtained by dividing one set of odds by another. The term "odds" or "odds ratio" is defined differently according to the situation under discussion. Consider the following notation for the distribution of a binary *exposure* and a disease in a population or a *sample*.

	<i>Exposed</i>	Nonexposed
Disease	<i>a</i>	<i>b</i>
No disease	<i>c</i>	<i>d</i>

The odds ratio (cross-product ratio) is ad/bc .

synonyms *cross-product ratio, relative odds*

Note 1: The *exposure-odds* ratio for a set of case control data is the ratio of the odds in favour of exposure among the cases (a/b) to the odds in favour of exposure among non-cases (c/d). This reduces to ad/bc . With incident cases, unbiased subject selection, and a "rare" disease (say, under 2 % cumulative *incidence* rate over the study period), ad/bc is an approximate estimate of the *risk* ratio. With incident cases, unbiased subject selection, and density sampling of controls, ad/bc is an estimate of the ratio of the person-time incidence rates (force of morbidity) in the *exposed* and unexposed. No rarity assumption is required for this.

Note 2: The disease-odds (rate-odds) ratio for a cohort or cross section is the ratio of the odds in favour of disease among the exposed population (a/c) to the odds in favour of disease among the unexposed (b/d). This reduces to ad/bc and hence is equal to the exposure-odds ratio for the cohort or cross section.

Note 3: The *prevalence-odds* ratio refers to an odds ratio derived cross sectionally, as, for example, an odds ratio derived from studies of prevalent (rather than incident) cases.

Note 4: The *risk-odds* ratio is the ratio of the odds in favour of getting disease, if exposed, to the odds in favour of getting disease if not *exposed*. The odds ratio derived from a cohort study is an estimate of this.

odor threshold

In principle, the lowest *concentration* of an odorant that can be detected by a human being; for a reference material, the odorant concentration which has a probability of 0.5 of being detected under the conditions of the test. [CEN TC264 Draft].

Note: In practice, a panel of "sniffers" is often used, and the threshold taken as the concentration at which 50 % of the panel can detect the odorant (although some workers have also used 100 % thresholds).

oedema

Presence of abnormally large amounts of fluid in intercellular spaces of body tissues.

olf

unit used to measure scent emission of people and objects; one olf is defined as the scent emission of an "average person", a sitting adult that takes an average of 0.7 baths per day and whose skin has a total area of 1,8 m²; the scent emission of an object or person is measured by specially trained personnel comparing it to normed scents.

Note: the olf should not be confused with the of unit of scent imission (as opposed to emission), the *decipol* which also takes into account the ventilation's air volume flow.

olfactometer

Apparatus for testing the power of the sense of smell.

oligozoospermia

Sperm concentration less than a reference value.

[6]

oliguria

Excretion of a diminished amount of urine in relation to fluid intake.

-omics, -omes

Neologism referring to the fields of study in biology ending in the suffix -omics, such as genomics or proteomics: the related neologism -omes are the objects of study of the field such as the genome or proteome, respectively.

oncogene

Gene that can cause neoplastic (see *neoplasia*) transformation of a cell; oncogenes are slightly changed equivalents of normal *genes* known as proto-oncogenes.

oncogenesis

Production or causation of *tumors*.

oncogenic

Capable of producing tumors in animals, either benign (non-cancerous) or malignant (cancerous).

[7]

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.

[2]

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.

onycholysis

Loosening or detachment of the nail from the nail bed following some destructive process.

oogenesis

Process of formation of the ovum (plural ova), the female *gamete*.

operon

Complete unit of *gene* expression and regulation, including structural *genes*, regulator *gene(s)* and control elements in *DNA* recognized by regulator *gene* product(s).

ophthalmic

Pertaining to the eye.

organ dose

Amount of a substance or physical agent (radiation) absorbed by an organ.

organelle

Microstructure or separated compartment within a cell that has a specialized function, for example ribosome, peroxisome, lysosome, Golgi apparatus, mitochondrion, nucleolus, nucleus.

organic carbon partition coefficient, K_{oc}

Measure of the tendency for organic substances to be adsorbed by soil and sediment, expressed as:

$$K_{oc} = \frac{(\text{mg substance adsorbed})/(\text{kg organic carbon})}{(\text{mg substance dissolved})/(\text{litre of solution})}$$

The K_{oc} is substance-specific and is largely independent of soil properties.

organoleptic

Involving an organ, especially a sense organ as of taste, smell or sight.

osteo-

Prefix meaning pertaining to bone.

osteodystrophy

Abnormal development of bone.

osteogenesis

Formation or development of bone.

osteomalacia

Condition marked by softening of the bones (due to impaired mineralisation, with excess accumulation of osteoid), with pain, tenderness, muscular weakness, anorexia and loss of weight, resulting from deficiency of vitamin D and calcium.

osteoporosis

Significant decrease in bone mass with increased porosity and increased tendency to fracture.

ovicide

Substance intended to kill eggs.

oxidative stress

Adverse effects occurring when the generation of reactive oxygen species (ROS) in a system exceeds the system's ability to neutralize and eliminate them; excess ROS can damage a cell's lipids, protein or DNA.

palpitation

1. Unduly rapid or throbbing heartbeat that is noted by a patient; it may be regular or irregular.
2. Undue awareness by a patient of a heartbeat that is otherwise normal.

paraesthesia

Abnormal sensation, as burning or prickling.

paralysis

Loss or impairment of motor function.

paralytic shellfish poisoning, PSP

Serious illness which is a consequence of consumption of toxic bivalve shellfish (mollusks) such as mussels, oysters and clams that have ingested, by filter feeding, large quantities of micro-algae containing saxitoxin; initially there is tingling, numbness and burning of the tongue and lips, which spreads to the face, neck, arms, fingertips, legs and toes and this is followed by weakness of the upper and lower limbs, loss of motor coordination and, in severe cases, paralysis.

para-occupational exposure

- 1 *Exposure* of a worker's family to substances carried from the workplace to the home.
2. Exposure of visitors to substances in the workplace.

parasympatholytic

Producing effects resembling those caused by interruption of the parasympathetic nerve; also called anticholinergic.

parasympathomimetic

Producing effects resembling those caused by stimulation of the parasympathetic nervous system.

Synonym *cholinomimetic*.

parenteral dosage

Method of introducing substances into an organism avoiding the gastrointestinal tract (subcutaneously, intravenously, intramuscularly etc.).

paresis

Slight or incomplete paralysis.

paresthesia

Abnormal or unexplained tingling, pricking, or burning sensation on the skin.

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.

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.

[2]

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 modelling purposes.

[2]

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.

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:

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

[2]

passive sampler

Device for taking samples of environmental media following diffusional contact with a suitable collecting material.

See *personal sampler*

passive smoking

Inhalation of sidestream smoke by people who do not smoke themselves.

See also *sidestream smoke*

patch test

Test for allergic sensitivity in which a suspected allergen is applied to the skin on a small surgical pad; may also be used to detect exposure to pesticides.

peak daily average concentration of an air pollutant

See synonym *maximum average daily concentration of an atmospheric pollutant*

penetration (in cell biology)

1. Action of entering or passing through a cell membrane.
2. Ability or power to enter or pass through a cell membrane.

perceived environment or risk

See synonym *subjective environment*

percutaneous

Through the skin following application on the skin.

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.

[2]

perinatal

Relating to the period shortly before and after birth, usually from the twentieth to the twenty-ninth week of gestation to one to four weeks after birth.

peritoneal dialysis

Method of artificial *detoxication* in which a *toxic* substance from the body is transferred into liquid that is instilled into the peritoneum.

Note: Effectively this represents the employment of the peritoneum surrounding the abdominal cavity as a dialysing membrane for the purpose of removing *waste* products or toxins accumulated as a result of *renal* failure.

permeability

Ability or power to enter or pass through a cell membrane.

Synonym *penetration* (definition 2)

permeability co-efficient

For a solute or other substances such as nanoparticles traversing a membrane, this co-efficient is expressed in $\text{cm}\cdot\text{s}^{-1}$; it is equivalent to a diffusion coefficient for a solute in a membrane divided by the thickness of the membrane.

permeable

Of a membrane, allowing a given substance to pass through. When applied to nonbiological membranes with no qualification, the term normally refers to water.

permeation

Action of entering or passing through a cell membrane.

Synonym *penetration* definition 1.

permissible-exposure-limit (PEL)

Recommendation by US OSHA for a *TWA concentration* that must not be exceeded during any 8-hour work shift of a 40h working week.

peroxisome

Organelle, similar to a lysosome, characterized by its content of catalase (EC 1.11.1.6), peroxidase (EC 1.11.1.7) and other oxidative enzymes.

persistence

Attribute of a substance that describes the length of time that the substance remains in a particular environment before it is physically removed or chemically or biologically

transformed.

persistent inorganic pollutants, PIPs

Inorganic chemicals that are stable in the environment, are liable to long-range transport, may bio-accumulate in human and animal tissue, and may have significant impacts on human health and the environment; they include such substances as arsenides, fluorides, cadmium and lead salts.

persistent organic pollutants, POPs

Organic chemicals that are stable in the environment, are liable to long-range transport, may bio-accumulate in human and animal tissue, and may have significant impacts on human health and the environment; they include such substances as dioxin, PCBs, DDT, and tributyltin oxide (TBTO).

Note: The Stockholm Convention on Persistent Organic Pollutants was adopted at a Conference of Plenipotentiaries held from 22 to 23 May 2001 in Stockholm, Sweden; by signing this convention, governments have agreed to take measures to eliminate or reduce the release of POPs into the environment.

personal monitoring

Type of environmental monitoring in which an individual's *exposure* to a substance is measured and evaluated.

Note: This is normally carried out using a personal *sampler*.

personal protective device, PPD

See synonym *personal-protective-equipment*

Alternative synonym *individual protective device*

personal protective equipment, PPE

Equipment (clothing, gloves, hard hat, respirator and so on) worn by an individual to prevent *exposure* to a potentially *toxic* substance

Synonyms *individual protective device, personal protective device*

personal sampler

Compact, portable instrument for individual air sampling, measuring, or both, the content of a harmful substance in the respiration zone of a working person.

Synonym *individual monitor*

See *passive sampler*

pest

Organism that may harm public *health*, that attacks food and other materials essential to mankind, or otherwise affects human beings adversely.

pesticide

A substance intended to kill pests.

Note: In common usage, any substance used for controlling, preventing, or destroying animal, microbiological or plant pests.

pesticide residue

Any substance or mixture of substances found in man or animals or in food and water following use of a pesticide: the term includes any specified derivatives, such as degradation and conversion products, metabolites, reaction products and impurities considered to be of toxicological significance.

phagocytosis

Process by which particulate material is endocytosed by a cell.

[2]

See also *endocytosis*, *pinocytosis*

pharmaceutical

Medicinal drug.

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*.

[2]

pharmacogenetics

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

[2]

pharmacogenomics

Methods and science permitting identification of the *genes* which influence individual variation in the efficacy or toxicity of therapeutic agents, and the application of this information in clinical practice.

[2]

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.

2. Study of such processes.

[2]

pharmacology

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

[2]

pharynx

Throat, the part of the digestive tract between the oesophagus below and the mouth and nasal cavities above and in front.

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.

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.

phase III reaction (of *biotransformation*)

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

[2]

phenome

Complete phenotypic description of an organism (by analogy with *genome*).

phenotype

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

pheromone

Substance used in olfactory communication between organisms of the same species eliciting a change in sexual or social behaviour.

Synonyms *ectohormone*, *fermone*

photo-irritation

Inflammation of the skin caused *exposure* to light, especially that due to *metabolites* formed in the skin by photolysis.

photo-oxidant

Substance able to cause oxidation when *exposed* to light of the appropriate wavelength.

photophobia

Abnormal visual intolerance of light.

photosensitization

Allergic reaction (see *allergy*) due to a metabolite formed by the influence of light.

photolysis

Cleavage of one or more covalent bonds in a molecular entity resulting from absorption of light, or a photochemical process in which such cleavage is an essential part.

[4]

phototoxicity

Adverse effects produced by *exposure* to light energy, especially those produced in the skin.

physical map

See *genetic map*

physiological availability

See *bioavailability*

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.

[2]

Synonym *toxicologically based pharmacokinetic modelling*

pinocytosis

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

[2]

piscicide

Substance intended to kill fish.

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*.

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, i.e. the cytoplasm.

plasma half-life

See synonym *elimination half-life*

plasmapheresis

Removal of blood from the body and centrifuging it to obtain *plasma* and packed red blood cells: the blood cells are resuspended in a physiologically compatible solution (usually type-specific fresh frozen plasma or albumin) and returned to the donor or injected into a patient who requires blood cells rather than whole blood.

plasmid

Autonomous self-replicating extra-chromosomal circular *DNA* molecule present in bacteria and yeast.

Note 1: Plasmids replicate autonomously each time a bacterium divides and are transmitted to the daughter cells.

Note 2: DNA segments are commonly cloned using plasmid vectors.

After [7]

pleura

Lining of the lung.

ploidy

Term indicating the number of sets of *chromosomes* present in an organism.

plumbism

Chronic poisoning caused by absorption of lead or lead salts.

Synonym *saturnism*

pneumoconiosis

Usually fibrosis of the lungs that develops owing to (prolonged) inhalation of inorganic or organic dusts.

Cause-specific types of pneumoconiosis:

1. anthracosis: from coal dust.
2. asbestosis: from asbestos dust.
3. byssinosis: from cotton dust.
4. siderosis: from iron dust.
5. silicosis: from silica dust.
6. stannosis: from tin dust.

pneumonitis

Inflammation of the lung.

point mutation

Reaction that changes a single base pair in *DNA*.

point source

Single *emission* source in a defined location.

poison (in toxicology)

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

poison-bearing

Containing a *poison*.

poisoning

Morbid condition produced by a *poison*.

Synonym *intoxication*

pollutant

Any undesirable solid, liquid or gaseous matter in a solid, liquid or gaseous environmental medium.

Note 1: 'Undesirability' is often *concentration*-dependent, low concentrations of most substances being tolerable or even essential in many cases.

Note 2: A primary pollutant is one emitted into the atmosphere, water, sediments or soil from an identifiable source.

Note 3: A secondary pollutant is a pollutant formed by chemical reaction in the atmosphere, water, sediments, or soil.

pollution

Introduction of *pollutants* into a solid, liquid, or gaseous environmental medium, the presence of pollutants in a solid, liquid, or gaseous environmental medium, or any undesirable modification of the composition of a solid, liquid or gaseous environmental medium.

polyclonal antibody

Antibody produced by a number of different cell types.

polydipsia

Chronic excessive thirst.

polymerase chain reaction, PCR

Technique by which specific DNA segments are amplified selectively using cycles of annealing, chain extension, and thermal dissociation.

After [7]

polymorphism (polymorphia) in metabolism

Interindividual variations in *metabolism* of endo- and *exogenous* compounds due to genetic influences, leading to enhanced side effects or *toxicity of drugs* (for example, poor versus fast metabolizers) or to different clinical effects (metabolism of steroid hormones).

polyuria

Excessive production and discharge of urine.

population (in statistics)

Totality of related items under consideration.

Note 1: A clearly defined part of a population is called a subpopulation. The term 'population segment' is sometimes used as a synonym for subpopulation.

Note 2: In the case of a random variable, the probability distribution is considered as defining the population of that variable.

population (in epidemiology)

Assemblage of individuals with defined characteristics.

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*.

[2]

population critical concentration, PCC

Concentration of a substance in the critical organ at which a specified percentage of the *exposed* population has reached the individual critical organ concentration.

Note: The percentage is indicated by PCC-10 for 10 %, PCC-50 for 50 % etc. (similar to the use of the term *LD50*).

population effect

Absolute number or *incidence* rate of cases occurring in a group of people.

population risk

See synonym *societal risk*

porphyria

Disturbance of porphyrin *metabolism* characterized by increased formation, accumulation, and excretion of porphyrins and their precursors.

posology

Study of *dose* in relation to the physiological factors that may influence response such as age of the *exposed* organisms.

post-translational modification

Processes by which proteins are biochemically modified within a cell following their synthesis in the ribosomes.

potency (in toxicology)

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

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.

practical certainty (of safety)

Numerically specified low *risk* of *exposure* to a potentially *toxic* substance (for example, 1 in 1000) or socially acceptable low risk of *adverse effects* from such an exposure applied to decision making in regard to chemical safety.

precautionary principle

The precautionary principle is an approach to risk management that can be applied in circumstances of scientific uncertainty, reflecting a perceived need to take action in the face of a potentially serious risk without waiting for results of scientific research. The 1992 Rio Declaration on Environment and Development says: *'In order to protect the environment, the precautionary approach shall be widely applied by states according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.'*

precision

Measure for the reproducibility of measurements within a set, that is, of the scatter or dispersion of a set about its central value.

precordial

Pertaining to the region over the heart and lower thorax.

precursor

Substance from which another, usually more biologically active, substance is formed.

predicted environmental concentration, PEC

See *estimated environmental concentration*

predicted no effect concentration, PNEC

Concentration that is expected to cause no adverse effect to any naturally occurring population in an environment at risk from exposure to a given substance.

predictive validity

Reliability of a measurement expressed in terms of its ability to predict the criterion: an example would be an academic aptitude test that was validated against subsequent academic performance.

predictive value

Percentage of positive results that are true positives or of negative results that are true negatives.

premature ovarian failure

Follicular depletion by the age of 35 years.

[6]

preneoplastic

Before the formation of a *tumour*.

prevalence

Number of instances of existing cases of a given disease or other condition in a given

population at a designated time; sometimes used to mean *prevalence rate*. When used without qualification, the term usually refers to the situation at a specified point in time (point prevalence).

prevalence rate (ratio)

Total number of individuals who have an attribute or disease at a particular time (or during a particular period) divided by the population at *risk* of having the attribute or disease at this point in time or midway through the period.

primary pollutant

See *pollutant*

prior informed consent, PIC

Concept in law and medicine which states that before one is subjected to a risk, especially a risk of bodily harm, one is entitled to be fully informed well in advance of the nature of that risk in order to make an informed decision about whether to accept it or not.

primary protection standard

Accepted maximum level of a *pollutant* (or its indicator) in the *target* organism, or some part thereof, or an accepted maximum intake of a pollutant or nuisance into the target under specified circumstances.

probit

Probability unit obtained by adding 5 to the normal deviates of a standardized normal distribution of results from a dose response study: addition of 5 removes the complication of handling negative values.

Note: A plot of probit against the logarithm of *dose* or *concentration* gives a linear plot if the distribution of response is a logarithmic normal one. Estimates of the *LD50* and *ED50* (or *LC50* and *EC50*) can be obtained from this plot.

procarcinogen

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

[2]

prodrug

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

[2]

prokaryote

Unicellular organism, characterised by the absence of a membrane-enclosed nucleus.

Prokaryotes include bacteria, blue-green algae and mycoplasmas.

promoter (in molecular genetics)

Sequence of nucleotides in a DNA molecule to which RNA polymerase binds so as to start transcription.

promoter (in oncology)

Agent that induces *cancer* when administered to an animal or human being who has been *exposed* to a *cancer initiator*.

promotor

Less common spelling of *promoter* (in molecular genetics), possibly spurious

pro-pesticide

Substance applied in a form that is not active as a pesticide and which becomes active once it enters an organism and undergoes chemical modification.

prophage

Latent state of a phage *genome* in a lysogenic bacterium.

proportional mortality rate (ratio)

Proportion of observed deaths from a specified condition in a defined population divided by the proportion of deaths expected from this condition in a standard population, expressed either on an age-specific basis or after age adjustment.

prospective cohort study

See *cohort study*

prosthetic group

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

[2]

proteinuria

Excretion of excessive amounts of protein (derived from blood *plasma* or kidney tubules) in the urine.

proteome

Description of the complete set of proteins encoded by the *genome*.

[2]

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.

[2]

pseudo-acceptable daily intake, PADI

Intake for a substance derived by applying a thousandfold uncertainty factor to the lowest

low-effect level for noncarcinogenic endpoints.

pseudoadaptation

Apparent adaptation of an organism to changing conditions of the environment (especially chemical) associated with stresses in biochemical systems that exceed the limits of normal (homeostatic) mechanisms.

Note: Essentially there is a temporary concealed pathology that later on can be manifested in the form of explicit pathological changes sometimes referred to as 'decompensation'.

psychosis

Any major mental disorder characterized by derangement of the personality and loss of contact with reality.

psychotropic

Exerting an effect upon the mind and capable of modifying mental activity.

public health impact assessment

Applying *risk* assessment to a specific target population of known size, giving as the end product a quantitative statement about the number of people likely to be affected in a particular population.

pulmonary

Pertaining to the lung(s).

[2]

purgative

See Synonym *laxative*

pyrexia

Condition in which the temperature of a human being or mammal is above normal.

pyrogen

Any substance that produces fever.

quality assurance

All those planned and systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality.

quality control

1. Operational techniques and activities that are used to fulfil requirements for quality.
2. In toxicology, procedures incorporated in experimental protocols to reduce the possibility of error, especially human error.

Note: This is a requirement of good laboratory practice.

quantal

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

[2]

quantal effect

Condition that can be expressed only as 'occurring' or 'not occurring', such as death or occurrence of a tumour.

Antonym *graded effect*

Synonym *all-or-none effect*

quantitative structure-activity relationship, QSAR

Quantitative structure-biological activity model 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-

[2]

quantitative structure *metabolism* relationship, QSMR

Quantitative association between the physicochemical and (or) the structural properties of a substance and its metabolic behaviour.

[2]

radiation toxicology

Scientific study involving research, education, prevention and treatment of diseases caused by ionizing radiation.

râles

See Synonym *crepitations*

random (probability) sample

Subset of units of a population that is arrived at by selecting units such that each possible unit has a fixed and known probability of selection.

Antonym *biased sample*

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.

[2]

rate constant, *k*

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

[2]

rate difference, RD

Absolute difference between two *rates*.

Note 1: For example, the difference in *incidence* rate between a population group *exposed* to a causal factor and a population group not exposed to the factor.

Note 2: In comparisons of exposed and unexposed groups, the term '*excess rate*' may be used as a synonym for rate difference.

rate-limiting step

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

[2]

rate ratio, RR (in epidemiology)

Value obtained by dividing the *rate* in an *exposed* population by the rate in an unexposed population.

ratticide

Substance intended to kill rats.

re-absorption (in biology)

Absorption by a living organism of a substance which it has previously absorbed and then released, e.g., the uptake of a substance from the proximal renal tubule following glomerular filtration.

reactive nitrogen species, RNS

radical nitrogen-based molecules that can act to facilitate nitrosylation reactions; reactive nitrogen species include: nitrogen dioxide NO_2^\bullet , nitrous oxide NO^\bullet , nitrosyl cation NO^+ , nitrous acid HNO_2 , and nitroxyl anion NO^- .

reactive oxygen species, ROS

Intermediates in the reduction of molecular O_2 to water.

Note: Examples are superoxide anion $\text{O}_2^{\bullet-}$, hydrogen peroxide H_2O_2 , and hydroxyl radical HO^\bullet .

[2]

readily biodegradable

Arbitrary classification of substances that have passed certain specified screening tests for ultimate biodegradability (see *biodegradation*); these tests are so stringent that such compounds will be rapidly and completely biodegraded in a wide variety of *aerobic* environments.

reasonable maximum exposure, RME

Highest *exposure* that is reasonably expected to occur.

Note: Typically the 95% upper confidence limit of the *toxicant* distribution is used: if only a few data points (6-10) are available, the maximum detected *concentration* is used.

recalcitrance

Ability of a substance to remain in a particular environment in an unchanged form.

receptor

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

[2]

receptor-mediated endocytosis

Endocytosis of a substance and its *receptor* following receptor binding.

[2]

recessive gene

Allele which in the heterozygous state is expected to have no effect on the phenotype of the organism which carries it.

After [7]

recombinant DNA technology

Methods involving the use of restriction enzymes to cleave DNA at specific sites, allowing sections of DNA molecules to be inserted into plasmid or other vectors and cloned in an appropriate host organism (e.g. a bacterial or yeast cell).

After [7]

reconstitution

Restoration to original form of a substance previously altered for preservation and storage.

[2]

recovery

1. Process leading to partial or complete restoration of a cell, tissue, organ or organism following its damage from *exposure* to a harmful substance or agent.
2. Term used in analytical and preparative chemistry to denote the fraction of the total quantity of a substance recoverable following a chemical procedure.

recovery factor

Fraction or percentage of the total quantity of a substance extracted under specified conditions.

recycling (of waste)

Process or method allowing for the recovery of some value from a *waste*, either as re-usable material or as energy.

reference concentration

Term used for an estimate of air *exposure concentration* to the human population (including sensitive subgroups) that is likely to be without appreciable *risk* of deleterious effects during a lifetime.

reference distribution

Statistical distribution of reference values.

reference concentration

Term used for an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily *exposure* (as a *concentration*) to the human population (including sensitive subgroups) that is likely to be without appreciable *risk* of deleterious effects during a lifetime.

reference dose, RfD

Term used for an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily *exposure* (as a *dose*) to the human population (including sensitive subgroups) that is likely to be without appreciable *risk* of deleterious effects during a lifetime.

reference group

See synonym *reference sample group*

reference individual

Person selected with the use of defined criteria for comparative purposes in a clinical study.

reference interval

Area between and including two reference limits, for example the percentiles 2.5 and 97.5.

reference limit

Boundary value defined so that a stated fraction of the reference values is less than or exceeds that boundary value with a stated probability.

reference material

Substance for which one or more properties are sufficiently well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to other substances.

Synonyms *calibration material*, *standard material*

reference population

Group of all reference individuals used to establish criteria against which a population that is being studied can be compared.

reference sample group

Selected reference individuals, statistically adequate numerically to represent the

reference population.

reference value

According to IFCC, measured value of a property in a reference individual or *sample* from a reference individual.

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.

[2]

regression analysis

Statistical methods for modelling a set of dependent variables, Y , in terms of combinations of predictors, X .

[2]

regulatory dose

Term used by the USEPA to describe the expected dose resulting from human *exposure* to a substance at the level at which it is regulated in the environment.

regulatory sequence

DNA sequence to which specific proteins bind to activate or repress the expression of a *gene*.

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.

[2]

relative odds

See synonym *odds ratio*

relative risk, RR

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*

relative systemic availability

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

[2]

renal

Pertaining to the kidneys.

[2]

renal plasma flow

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

[2]

repeatability

Closeness of agreement between independent results obtained with the same method on identical test material, under the same conditions (same operator, same apparatus, same laboratory and after short intervals of time). The *measure of repeatability* is the standard deviation. In some contexts, repeatability may be defined as the value below which the absolute difference between two single test results obtained under the above conditions, may be expected to lie within a specified probability.

[4]

repellent

Substance used mainly to repel blood sucking insects in order to protect man and animals.

Note: This term may also be used for substances used to repel mammals, birds, rodents, mites, plant pests, etc.

replicate sampling

Act of taking multiple *samples* concurrently under comparable conditions.

Note: Replicate sampling may be accomplished by taking samples adjacent in time or space.

replication

1. Duplicated or repeated performance of an experiment under similar (controlled) conditions to reduce to a minimum the error, and to estimate the variations and thus obtain a more precise result: each determination, including the first is called a replicate.
2. Process whereby the genetic material is duplicated.

reproducibility

Closeness of agreement between test results obtained under *reproducibility conditions* (*see below*).

reproducibility conditions

Situation where test results are obtained with the same method on identical test material in different laboratories with different operators using different equipment.

reproductive toxicant

Substance or preparation that produces non-heritable harmful effects on the progeny and (or) an impairment of male and female reproductive function or capacity.

reproductive toxicology

Study of the *adverse effects* of substances on the embryo, fetus, neonate and prepubertal mammal and the adult reproductive and neuro-endocrine systems.

reserve capacity

Physiological or biochemical capacity that may be available to maintain homeostasis when the body or an organism is *exposed* to an environmental change.

reservoir (in biology)

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

[2]

residence time

See *mean residence time*

residual risk

Health risk remaining after risk reduction actions are implemented.

[2]

residual time

See *mean residence time*

residue

Contaminant remaining in an organism or in other material such as food or packaging, following exposure.

resistance (in toxicology)

Ability to withstand the effect of various factors including potentially *toxic* substances.

resorption

1. Synonym for *re-absorption*
2. (in biology) Process in which the components of some differentiated structure that has been produced by the body undergo lysis and assimilation.

resorptive effect

Action of a substance after its resorption from the gut into the blood.

respirable dust

Mass fraction of dust (particles) that penetrates to the unciliated airways of the lung (the alveolar region).

Note: This fraction 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).

[2]

Synonym *respirable particles*

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.

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.

retrospective study

Research design used to test aetiological hypotheses in which inferences about *exposure* to the putative causal factor(s) are derived from data relating to characteristics of the persons or organisms under study or to events or experiences in their past.

Note: The essential feature is that some of the persons under study have the disease or other outcome condition of interest, and their characteristics and past experiences are compared with those of other, unaffected persons. Persons who differ in the severity of the disease may also be compared.

returned effect of poisons

Enhancement of the *dose-effect* relationship for a poison following repeated *exposure* to decreasing doses.

reverse transcription

Process by which an *RNA* molecule is used as a template to make a single-stranded *DNA* copy.

reversible alteration

Change from normal structure or function, induced by a substance or other agent(s), that returns to normal status or within normal limits after cessation of *exposure*.

rhabdomyolysis

Acute, fulminating, potentially lethal disease of skeletal muscle that causes disintegration of striated muscle fibres as evidenced by myoglobin in the blood and urine.

rhinitis

Inflammation of the nasal mucosa.

rhonch/us (pl -i)

Harsh crepitation in the throat, often resembling snoring.

ribonucleic acid, RNA

Linear, usually single stranded, polymer of ribonucleotides, each containing the sugar ribose in association with a phosphate group and one of 4 nitrogenous bases: adenine, guanine, cytosine, or uracil.

Note: RNA encodes the information for the sequence of amino-acids in proteins synthesized using it as a template.

risk

1. Probability of *adverse effects* caused under specified circumstances by an agent in an organism, a population or an ecological system.
2. Probability of a hazard causing an *adverse effect*.
3. Expected frequency of occurrence of a harmful event arising from such an *exposure*.

After [2]

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.

risk assessment management process

Global term for the whole process from *hazard* identification to *risk* management.

risk associated with a life time exposure

Probability of the occurrence of a specified undesirable event following *exposure* of an individual person from a given population to a specified substance at a defined level for the expected lifetime of the average member of that population.

risk aversion

Term used to describe the tendency of an individual person to avoid *risk*.

risk characterization

Outcome of *hazard* identification and *risk* estimation applied to a specific use of a substance or occurrence of an environmental *health* hazard.

Note: Risk characterization requires quantitative data on the *exposure* of organisms or people at *risk* in the specific situation. The end product is a quantitative statement about the proportion of organisms or people affected in a target population.

risk communication

Interpretation and communication of *risk* assessments in terms that are comprehensible to the general public or to others without specialist knowledge.

risk de minimis

Risk that is negligible and too small to be of societal concern (usually assumed to be a probability below 10^{-5} or 10^{-6}).

Note 1: This term can also mean ‘virtually safe’.

Note 2: In the USA, this is a legal term used to mean ‘negligible *risk* to the individual’.

Synonym *negligible risk*

risk estimation

Assessment, with or without mathematical modelling, of the probability and nature of effects of *exposure* to a substance based on quantification of *dose-effect* and *dose-response* relationships for that substance and the population(s) and environmental components likely to be *exposed* and on assessment of the levels of potential exposure of people, organisms and environment at *risk*.

risk evaluation

Establishment of a qualitative or quantitative relationship between *risks* and benefits, involving the complex process of determining the significance of the identified *hazards* and estimated risks to those organisms or people concerned with or affected by them.

risk identification

Recognition of a potential *hazard* and definition of the factors required to assess the probability of *exposure* of organisms or people to that hazard and of harm resulting from such exposure.

risk indicator

See synonym *risk marker*

risk management

Decision-making process involving considerations of political, social, economic, and engineering factors with relevant *risk* assessments relating to a potential *hazard* so as to develop, analyse, and compare regulatory options and to select the optimal regulatory response for safety from that hazard.

Note: Essentially risk management is the combination of three steps: *risk evaluation*; *emission* and *exposure* control; *risk monitoring*.

risk marker

Attribute that is associated with an increased probability of occurrence of a disease or other specified outcome and that can be used as an indicator of this increased *risk*.

Note: A risk marker is not necessarily a causal factor.

Synonym *risk indicator*

risk monitoring

Process of following up the decisions and actions within *risk management* in order to check whether the aims of reduced *exposure* and risk are achieved.

risk perception

Subjective perception of the gravity or importance of the *risk* based on a person's knowledge of different risks and the moral, economic, and political judgement of their implications.

risk phrases

Word groups identifying potential *health* or environmental *hazards* required under CPL Directives (European Community); may be incorporated into *Safety* Data Sheets.

risk quotient

Ratio of *predicted exposure concentration* to *predicted no effect concentration*: the higher this value above one, the greater the risk. If the value is below one, there should be no risk as a result of the predicted exposure.

risk ratio

Value obtained by dividing the probability of occurrence of a specific effect in one group by the probability of occurrence of the same effect in another group, or the value obtained by dividing the probability of occurrence of one potentially hazardous event by the probability of occurrence of another.

Note: Calculation of such ratios is used in choosing between options in *risk management*.

risk-specific dose

Amount of *exposure* corresponding to a specified level of *risk*.

rodenticide

Substance intended to kill rodents.

route of exposure

Means by which a *toxic* agent gains access to an organism by administration through the gastrointestinal tract (ingestion), lungs (inhalation), skin (topical), or by other routes such as intravenous, subcutaneous, intramuscular or intraperitoneal routes.

safety

Reciprocal of *risk*: practical certainty that injury will not result from a *hazard* under defined conditions.

1. Safety of a *drug* or other substance in the context of human *health*: the extent to which a substance may be used in the amount necessary for the intended purpose with a minimum risk of adverse health effects.
2. Safety (toxicological): The high probability that injury will not result from *exposure* to a substance under defined conditions of quantity and manner of use, ideally controlled to minimize exposure.

safety data sheet

Single page giving toxicological and other *safety* advice, usually associated with a particular preparation, substance or process.

safety factor, SF

See synonym *uncertainty factor*

saluretic

See synonym *natriuretic*

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

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.

[2]

sarcoma

Malignant tumour arising in a connective tissue and composed primarily of anaplastic cells resembling supportive tissue (see anaplasia).

saturable elimination

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

[2]

saturnism

Intoxication caused by lead.

Synonym *plumbism*

Scatchard plot

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

[2]

scotoma

Area of depressed vision within the visual field, surrounded by an area of less depressed or normal vision.

sclerosis

Hardening of an organ or tissue, especially that due to excessive growth of fibrous tissue.

screening

1. Carrying out of a test or tests, examination(s) or procedure(s) in order to expose undetected abnormalities, unrecognized (incipient) diseases, or defects: examples are mass X-rays and cervical smears.
2. Pharmacological or toxicological screening consists of a specified set of procedures to which a series of compounds is subjected to characterize pharmacological and toxicological properties and to establish *dose-effect* and *dose-response* relationships.

screening level

Decision limit or cut-off point at which a *screening* test is regarded as positive.

secondary metabolite

Product of biochemical processes other than the normal metabolic pathways, mostly produced in micro-organisms or plants after the phase of active growth and under conditions of nutrient deficiency.

secondhand smoke

See synonym *sidestream smoke*

second messenger

Intracellular effector substance increasing or decreasing as a result of the stimulation of a *receptor* by an *agonist*, considered as the 'first messenger'.

[2]

secretion

1. Process by which a substance such as a hormone or enzyme produced in a cell is passed through a *plasma membrane* to the outside, for example the intestinal lumen or the blood (internal secretion).
2. Solid, liquid or gaseous material passed from the inside of a cell through a plasma membrane to the outside as a result of cell activity.

sedative

Substance that exerts a soothing or tranquillising effect.

self-cleaning of water (in a reservoir)

Water purification by natural biological and physico-chemical processes.

self-purification of the atmosphere

Purification of the atmosphere from contaminants by natural biological and physico-chemical processes.

semichronic

See synonym *subchronic*

semiochemical

Substance produced by plants or animals, or a synthetic analogue thereof, that evokes a behavioural response in individuals of the producing species or other species (e.g. allomones, kairomones, pheromones, and synomones).

semipermeable (selectively or differentially permeable) membrane

Membrane that will preferentially allow certain molecules or ions to pass through it while preventing the passage of others.

sensibilization

See synonym *sensitization*

sensitivity (in analytical chemistry)

Extent to which a small change in *concentration* of an analyte can cause a large change in the related measurement.

sensitivity (of a screening test)

Extent (usually expressed as a percentage) to which a method gives results that are free from false negatives.

Note 1: The fewer the false negatives, the greater the sensitivity.

Note 2: Quantitatively, sensitivity is the proportion of truly diseased persons in the screened population who are identified as diseased by the screening test.

sensitization

Immune response whereby individuals become *hypersensitive* to substances, pollen, dandruff, or other agents that make them develop a potentially harmful *allergy* when they are subsequently *exposed* to the sensitizing material (*allergen*).

sensory effect level

1. Intensity, where the detection *threshold* level is defined as the lower limit of the perceived intensity range (by convention the lowest *concentration* that can be detected in 50 % of the cases in which it is present).

2. Quality, where the recognition threshold level is defined as the lowest concentration at which the sensory effect can be recognized correctly in 50 % of the cases.

3. Acceptability and annoyance, where the nuisance threshold level is defined as the *concentration* at which not more than a small proportion of the population, less than 5 %, experiences annoyance for a small part of the time, less than 2 %.

Note: Since annoyance will be influenced by a number of factors, a nuisance threshold level cannot be set on the basis of concentration alone.

serum

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

[2]

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.

short term effect

See synonym *acute effect*

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-hour TWA is within the *threshold limit value-time-weighted average*, TLV-TWA.

[2]

short-term toxicity

Synonym for *acute toxicity*.

side-effect

Action of a *drug* other than that desired for beneficial pharmacological effect.

siderosis

1. *Pneumoconiosis* resulting from the inhalation of iron dust.
2. Excess of iron in the urine, blood or tissues, characterized by haemosiderin granules in urine and iron deposits in tissues.

sidestream smoke

Cloud of small particles and gases that is given off from the end of a burning tobacco product (cigarette, pipe, cigar) between puffs and is not directly inhaled by the smoker.

Note: This is the smoke that gives rise to passive inhalation on the part of bystanders.

Synonyms *environmental tobacco smoke* (ETS), *secondhand smoke*

sign

Objective evidence of a disease, deformity or an effect induced by an agent, perceptible to an examining physician.

signal transduction

Molecular pathways through which a cell senses changes in its external or internal environment and changes its pattern of *gene* expression or enzyme activity in response.

After [7]

silicosis

Pneumoconiosis resulting from inhalation of silica dust.

simulation test

Procedure designed to predict the rate of *biodegradation* of a compound under relevant environmental conditions.

single nucleotide polymorphism, SNP

Single base variation at a chromosomal locus which exists stably within populations (typically defined as each variant form being present in at least 1-2% of individuals).

After [7]

sink

In environmental chemistry, an area or part of the environment in which, or a process by which, one or more *pollutants* is removed from the medium in which it is dispersed.

Note: For example - moist ground acts as a sink for sulfur dioxide in the air.

sister chromatid exchange, SCE

Reciprocal exchange of *chromatin* between two replicated *chromosomes* that remain attached to each other until anaphase of *mitosis*; used as a measure of *mutagenicity* of substances that produce this effect.

skeletal fluorosis

Osteosclerosis due to fluoride.

slimicide

Substance intended to kill slime-producing organisms (used on paper stock, water cooling systems, paving stones etc.).

slope factor

Value, in inverse *concentration* or *dose* units, derived from the slope of a *dose-response* curve; in practice, limited to *carcinogenic* effects with the curve assumed to be linear at low concentrations or doses.

Note: The product of the slope factor and the *exposure* is taken to reflect the probability of producing the related effect.

societal risk

Total probability of harm to a human population including the probability of *adverse effects* to *health* of descendants and the probability of disruption resulting from loss of services such as industrial plant or loss of material goods and electricity.

soil partition coefficient (soil K_d)

Experimental ratio of a substance's concentration in the soil to that in the aqueous (dissolved) soil phase at equilibrium: it is valid only for the specific concentration and solid/solution ratio of the test.

See *organic carbon partition coefficient*

[5]

solvent abuse

Deliberate inhalation (or drinking) of volatile solvents, in order to become intoxicated.

Synonym '*solvent sniffing*'

'solvent sniffing'

See synonym *solvent abuse*

somatic

1. Pertaining to the body as opposed to the mind.

2. Pertaining to nonreproductive cells or tissues.
3. Pertaining to the framework of the body as opposed to the viscera.

soporific

Substance producing sleep.

sorption

Noncommittal term used instead of *adsorption* or *absorption* when it is difficult to discriminate experimentally between these two processes.

speciation (in chemistry)

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

[2]

speciation analysis (in chemistry)

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

[2]

species

1. In biological systematics, group of organisms of common ancestry that are able to reproduce only among themselves and that are usually geographically distinct.
2. See *chemical species*

species differences in sensitivity

Quantitative or qualitative differences of response to the action(s) of a potentially *toxic* substance on various species of living organisms.

species-specific sensitivity

Quantitative and qualitative features of response to the action(s) of a potentially *toxic* substance that are characteristic for particular species of living organism.

specific death rate

Death rate computed for a subpopulation of individual organisms or people having a specified characteristic or attribute, and named accordingly.

Note: For example, age-specific death rate, the number of deaths of persons of a specified age during a given period of time, divided by the total number of persons of that age in the population during that time.

specificity (of a screening test)

Proportion of truly non-diseased persons who are identified by the screening test.

specific pathogen free, SPF

Describing an animal removed from its mother under sterile conditions just prior to term and subsequently reared and kept under sterile conditions.

specimen

Specifically selected portion of any substance, material, organism (specifically tissue, blood, urine or faeces) or environmental medium assumed to be representative of the parent substance etc. at the time it is taken for the purpose of diagnosis, identification, study or demonstration.

splicing

Processes through which introns are removed from a messenger RNA prior to translation and the exons joined.

[7]

spreader

Agent used in some *pesticide* formulations to extend the even disposition of the active ingredient.

stability half-life (half-time)

Time required for the amount of a substance in a formulation to decrease, for any reason, by one-half (50 %).

standard

1. That which is established as a measure or model to which others of a similar nature should conform.
2. Technical specification, usually in the form of a document available to the public, drawn up with the consensus or general approval of all interests affected by it, based on the consolidated results of science, technology and experience, aimed at the promotion of optimum community benefits and approved by a body recognized on the national, regional or international level.

Synonym *technical directive*

3. Reference substance.

Synonym *standard material*

standardization

1. Making any substance, *drug* or other preparation conform to type or precisely defined characteristics.
2. Establishment of precisely defined characteristics, or precisely defined methods, for future reference.
3. Definition of precise procedures for administering, scoring and evaluating the results of a new method that is under development.

standard material (in analytical chemistry)

1. Reference material (or calibration material) for which, for specified element *concentrations*, values are recommended by some official body.
2. Substance sufficiently well defined to be used for calibration and quality control of measurement techniques.

standard(ized) mortality (morbidity) ratio, SMR

Ratio of the number of deaths observed in the study group or population to the number of deaths that would be expected if the study population had the same specific rates as the standard population, multiplied by 100.

Note: This ratio is usually expressed as a percentage.

stannosis

Pneumoconiosis resulting from inhalation of tin dust.

steady state (in chemistry and toxicology)

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

[2]

stem cell

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

[2]

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.

[2]

stereoselectivity

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

[2]

stochastic

Pertaining to or arising from chance and hence obeying the laws of probability.

stochastic effect

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

Synonym *stochastic process*

stochastic process

See synonym *stochastic effect*

stratification (in epidemiology)

Process of or result of separating a *sample* into several subsamples according to specified criteria such as age groups, socio-economic status, etc.

stratified sample

Subset of a population selected according to some important characteristic.

structural alert

Chemical grouping which is known to be associated with a particular type of toxic effect, e.g. mutagenicity.

New definition

structure activity relationship, SAR

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

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 behaviour.

[2]

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.

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.

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.

subclinical effect

Biological change following *exposure* to an agent known to cause disease either before symptoms of the disease occur or when they are absent.

subfertility

Fertility below the normal range for a given species.

[6]

subjective environment

Surrounding conditions as perceived by persons living in these conditions.

Synonym *perceived environment*

subthreshold dose

See synonym *non-effective dose*

sudorific

Substance that causes sweating.

sufficient evidence

According to the USEPA's Guidelines for *Carcinogen Risk Assessment*, sufficient evidence is a collection of facts and scientific references that is definite enough to establish that an *adverse effect* is caused by the agent in question.

suggested no adverse response level (SNARL)

Maximum *dose* or *concentration* that on current understanding is likely to be tolerated by an *exposed* organism without producing any harm.

suicide reaction

Formation of irreversible cleavage complexes (also referred to as 'suicide complexes') leading to cell death.

summary sheet

Two-to-four page summary of a *risk assessment*.

summation (in neurophysiology)

Process of addition of separate postsynaptic responses caused by stimuli that are adjacent in time and space.

Note: Excitation of a synapse evokes a graded potential change in the postsynaptic membrane that may be below the threshold required to trigger an impulse. If two or more such potentials are caused either nearly simultaneously, at different synapses on the same neurone (spatial summation), or in rapid succession at the same synapse (temporal summation), the summed response may be sufficient to trigger a postsynaptic impulse. Summation may occur between excitatory potentials, inhibitory potentials, or between an excitatory and an inhibitory potential.

Superfund

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

super-threshold dose

See *toxic dose*

surface layer

Region of space comprising and adjoining the phase boundary between a solid and liquid

phase, between a solid and gas phase, or between a liquid and gas phase within which properties of matter are significantly different from the values in the adjoining bulk phases.

surrogate

Relatively well studied *toxicant* whose properties are assumed to apply to an entire chemically and toxicologically related class; for example, benzo(a)pyrene data may be used as toxicologically equivalent to that for all *carcinogenic* polynuclear aromatic hydrocarbons.

surveillance

Systematic ongoing collection, collation, and analysis of data and the timely dissemination of information to those who need to know in order that action can be taken to initiate investigative or control measures.

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.

[2]

Synonym vulnerable

susceptibility

Condition of lacking the power to resist a particular disease or infection; thus in susceptible people 'normal expected' results occur but with a lower *exposure* (or *dose*) than in the rest of the population.

sympatholytic

1. adj., Blocking transmission of impulses from the adrenergic (sympathetic) postganglionic fibres to effector organs or tissues.

2. n., Agent that blocks transmission of impulses from the adrenergic (sympathetic) postganglionic fibres to effector organs or tissues.

Synonym *anti-adrenergic*

sympathomimetic

1. adj., Producing effects resembling those of impulses transmitted by the postganglionic fibres of the sympathetic nervous system.

2. n., Agent that produces effects resembling those of impulses transmitted by the postganglionic fibres of the sympathetic nervous system.

Synonym *adrenergic*

symptom

Any subjective evidence of a disease or an effect induced by a substance as perceived by the affected subject.

symptomatology

General description of all of the signs and symptoms of *exposure* to a *toxicant*

Note: Signs are the overt (observable) responses associated with exposure (such as convulsions, death, etc.) whereas symptoms are covert (subjective) responses (such as nausea, headache, etc.).

synapse

Functional junction between two neurones, where a nerve impulse is transmitted from one neurone to another.

synaptic transmission

See *synapse*

syndrome

Set of signs and symptoms occurring together and often characterizing a particular disease-like state.

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.

synergist (in toxicology)

Substance which contributes more than additively to a mutual effect with another substance.

synergistic effect

See *synergism*

synomone

Semiochemical that is produced by one organism inducing a response in an organism of another species that is favourable to both the emitter and the responding organism.

See *allomone*, *kairomone*

synteny

Property of *genes* which reside on the same chromosome.

systematic sample

Subset selected according to some simple rule such as specified date or alphabetic classification.

systemic

1. Relating to the body as a whole.
2. Occurring at a site in the body remote from the point of contact with a substance.

After [1]

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.

systems biology

Study of the mechanisms underlying complex biological processes as integrated systems of many, diverse, interacting components; it involves (1) collection of large sets of experimental data (by high-throughput technologies and/or by mining the literature of reductionist molecular biology and biochemistry), (2) proposal of mathematical models that might account for at least some significant aspects of this data set, (3) accurate computer solution of the mathematical equations to obtain numerical predictions, and (4) assessment of the quality of the model by comparing numerical simulations with the experimental data.

tachy-

Prefix meaning rapid as in *tachycardia* and *tachypnoea*.

tachycardia

Abnormally fast heartbeat.
antonym *bradycardia*

tachypnoea

Abnormally fast breathing.
antonym *bradypnoea*

taeniocide

Substance intended to kill tapeworms.

target (in biology)

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

target population (epidemiology)

1. Collection of individuals, items, measurements, etc. about which inferences are required: the term is sometimes used to indicate the population from which a *sample* is drawn and sometimes to denote any reference population about which inferences are needed.
2. Group of persons for whom an intervention is planned.

T cell

See synonym *T lymphocyte*

technical directive

See *standard*

telomere

Structure which terminates the arm of a chromosome.

temporary acceptable daily intake

Value for the acceptable daily intake proposed for guidance when data are sufficient to conclude that use of the substance is safe over the relatively short period of time required to generate and evaluate further safety data, but are insufficient to conclude that use of the substance is safe over a lifetime.

Note: A higher-than-normal safety factor is used when establishing a temporary ADI and an expiration date is established by which time appropriate data to resolve the safety issue should be available.

temporary maximum residue limit

Regulatory value established for a specified, limited time when only a temporary acceptable daily intake has been established for the *pesticide* concerned or, with the existence of an agreed acceptable daily intake, the available residue data are inadequate for firm maximum residue recommendations.

teratogen

Agent that, when administered prenatally (to the mother), induces permanent structural malformations or defects in the offspring.

teratogenicity

Potential to cause or the production of structural malformations or defects in offspring.

testing of chemicals

1. In *toxicology*, evaluation of the therapeutic and potentially *toxic* effects of substances by their application through relevant routes of *exposure* with appropriate organisms or biological systems so as to relate effects to *dose* following application.
2. In chemistry, qualitative or quantitative analysis by the application of one or more fixed methods and comparison of the results with established standards.

tetanic

Pertaining to tetanus, characterized by tonic muscle spasm.

theoretical maximum daily intake, TMDI

Predicted maximum daily intake of a residue, assuming that it is present at the *maximum residue level* and that average daily consumption of foods per person is represented by assessed regional diets: it is expressed in milligrams of residue per person per day.

After [11]

therapeutic cloning

Generation and manipulation of stem cells with the objective of deriving cells of a particular organ or tissue to treat a disease.

therapeutic index

Ratio between *toxic* and therapeutic doses (the higher the ratio, the greater the safety of the therapeutic dose).

three-dimensional quantitative structure-activity relationship, 3D-QSAR

Quantitative association between the three-dimensional structural properties of a substance and its biological properties.

[2]

See *quantitative structure-activity relationship*

threshold

Dose or *exposure concentration* below which a defined effect will not occur.

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-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]

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*.

[2]

threshold of toxicological concern, TTC

Human exposure threshold value for a group of chemicals below which there should be no appreciable risk to human health.

thrombocytopenia

Decrease in the number of blood platelets (thrombocytes).

tidal volume

Quantity of air or test gas that is inhaled and exhaled during one respiratory cycle.

time-weighted-average-exposure, TWAE, or concentration, TWAC

Concentration in the *exposure* medium at each measured time interval multiplied by that time interval and divided by the total time of observation

Note: For occupational exposure a working shift of eight hours is commonly used as the averaging time.

tinnitus

Continual noise in the ears, such as ringing, buzzing, roaring, or clicking.

tissue dose

Amount of a substance or physical agent (radiation) absorbed by a tissue.

tissue/plasma partition coefficient

See *partition ratio*

T lymphocyte

Animal cell which possesses specific cell surface *receptors* through which it binds to foreign substances or organisms, or those which it identifies as foreign, and which initiates *immune responses*.

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* is normally used for substances not known to be harmful, such as food additives.

[2]

tolerable risk

Probability of suffering disease or injury that can, for the time being, be tolerated, taking into account the associated benefits, and assuming that the *risk* is minimized by appropriate control procedures.

tolerable weekly intake, TWI

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

[2]

tolerance

1. Adaptive state characterized by diminished effects of a particular *dose* of a substance: the process leading to tolerance is called "adaptation."

2. In food *toxicology*, dose that an individual can tolerate without showing an effect.
3. Ability to experience *exposure* to potentially harmful amounts of a substance without showing an *adverse effect*.
4. Ability of an organism to survive in the presence of a *toxic* substance: increased tolerance may be acquired by adaptation to constant *exposure*.
5. In immunology, state of specific immunological unresponsiveness.

tonic

1. Characterised by tension, especially muscular tension.
2. Medical preparation that increases or restores normal muscular tension.

topical (in medicine)

Applied directly to the surface of the body.

[2]

topical effect

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

[2]

total diet study

1. Study designed to establish the pattern of *pesticide* residue intake by a person consuming a defined diet.
2. Study undertaken to show the range and amount of various foodstuffs in the typical diet or to estimate the total amount of a specific substance in a typical diet.

total terminal residue (of a pesticide)

Summation of levels of all the residues of a defined pesticide in a food.

See *residue*

After [5]

toxic

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

toxicant

See synonym *toxic substance*

toxic chemical

See synonym *toxic substance*

toxic dose

Amount of a substance which produces intoxication without lethal outcome.

Synonym *super-threshold dose*

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* ($1/LC_{50}$).

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 for which the TEF = 1.

toxicity equivalency factor, TEF, f

Ratio of the toxicity of a chemical to that of another structurally related chemical (or index compound) chosen as a reference.

[5]

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. 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:

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

toxic substance

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

[2]

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

toxicity exposure ratio, TER

Ratio of the measure of the effects (e.g., LD_{50} , LC_{50} , NOEC) to the estimated exposure.

Note: It is the reciprocal of a *risk quotient* or *hazard quotient*.

[5]

toxicity test

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

toxic material

See synonym *toxic substance*

toxicodynamics

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

toxicogenomics

Scientific sub-discipline that combines *toxicology* with *genomics* to determine how an organism's genetic make-up influences its response to a toxic substance.

toxicogenetics

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

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.

toxicological data sheet

Document that gives in a uniform manner data relating to the *toxicology* of a substance, its production and application, properties and methods of identification.

Note: The data sheet may also include recommendations on protective measures.

toxicologically based pharmacokinetic modelling, TBPK

See *physiologically based pharmacokinetic modelling*

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.

toxicometry

Term sometimes used to indicate a combination of investigative methods and techniques for making a quantitative assessment of *toxicity* and the *hazards* of potentially *toxic substances*.

toxicophobia

Morbid dread of *poisons*.

toxicophoric (toxophoric) group

Structural moiety that upon metabolic activation exerts *toxic effects*: the presence of a toxicophoric group indicates only potential and not necessarily actual *toxicity* of a *drug* or other substances.

Synonym *toxogenic group*

toxicovigilance

Active process of identification, investigation, and evaluation of various *toxic* effects in the community with a view to taking measures to reduce or control *exposure(s)* involving the substance(s) which produces these effects.

toxic substance

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

Synonyms *chemical etiologic agent, poison, toxicant, toxic chemical, toxic material*

toxification

Metabolic conversion of a potentially *toxic* substance to a product that is more toxic.

toxin

Poisonous substance produced by a biological organism such as a microbe, animal, plant or fungus.

toxinology

Scientific discipline involving the study of the chemistry, biochemistry, pharmacology and *toxicology* of *toxins*.

toxogenic group

Synonym *toxicophoric group*

tracer

1. Means by which something may be followed; for example a radioactive isotope may replace a stable chemical element in a *toxic* compound enabling the toxicokinetics to be followed.
2. Labelled member of a population used to measure certain properties of that population.

tracer substance

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

[2]

transcription

Process by which the genetic information encoded in a linear sequence of nucleotides in one strand of *DNA* is copied into an exactly complementary sequence of *RNA*.

transcriptome

Total messenger RNA expressed in a cell or tissue at a given point in time.

transcriptomics

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

[2]

transformation

1. Alteration of a cell by incorporation of foreign genetic material and its subsequent expression in a new *phenotype*.
2. Conversion of cells growing normally to a state of rapid division in culture resembling that of a *tumour*.
3. Chemical modification of substances in the environment.

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.

[2]

transformed cell line

See *cell line, transformed cell*

transgene

Gene from one source that has been incorporated into the genome of another organism.

transgenic

Adjective used to describe animals carrying a *gene* introduced by micro-injecting *DNA* into the nucleus of the fertilized egg.

translation

Process through which a polypeptide chain of amino acid molecules is generated as directed by the sequence of a particular messenger RNA sequence.

transposon

Mobile nucleic acid element.

treatability

In relation to *waste* water, the amenability of substances to removal without adversely affecting the normal operation of biological treatment processes (such as a sewage treatment plant).

triage

Assessment of sick, wounded and injured persons following a disaster to determine priority needs for efficient use of available medical facilities.

trophic level

Amount of energy in terms of food that an organism needs.

Note: Organisms not needing organic food, such as plants, are said to be on a low trophic level, whereas predator species needing food of high energy content are said to be on a high trophic level. The trophic level indicates the level of the organism in the food chain.

tubular reabsorption

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

[2]

tumorigenic

Able to cause *tumours*.

tumour

1. Any abnormal swelling or growth of tissue, whether benign or malignant.
2. An abnormal growth, in rate and structure, that arises from normal tissue, but serves no physiological function.

Synonym *neoplasm*

tumour progression

Sequence of changes by which a *benign tumour* develops from the initial lesion to a *malignant* stage.

tumour suppressor gene

Gene which serves to protect cells from entering a cancerous state.

Note: According to Knudson's "two-hit" hypothesis, both alleles of a particular tumour suppressor *gene* must acquire a mutation before the cell will enter a transformed state.

turnover time

See synonym *mean life*

two-compartment model

Product of *compartmental analysis* requiring two *compartments*.

[2]

See *compartmental modelling, multicompartment analysis*

ulcer

Defect, often associated with *inflammation*, occurring locally or at the surface of an organ or tissue owing to sloughing of necrotic (see *necrosis*) tissue.

ultrafine particles

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

[2]

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 to calculate the ADI or TDI.

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 interpretation of unit risk is as follows: if unit risk = $1.5 \times 10^{-6} \mu\text{g L}^{-1}$, 1.5 excess tumours are expected to develop per 1,000,000 people if exposed daily for a lifetime to $1 \mu\text{g}$ of the chemical in 1 litre of drinking water.

upper boundary

Estimate of the plausible upper limit to the true value of a quantity.

Note: This is usually not a statistical confidence limit.

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.

urticaria

Vascular reaction of the skin marked by the transient appearance of smooth, slightly elevated patches (wheals, hives) that are redder or paler than the surrounding skin and often attended by severe itching.

vacuole

Membrane-bound cavity within a cell.

validity (of a measurement)

Expression of the degree to which a measurement measures what it purports to measure.

validity (of a study)

Degree to which the inferences drawn, especially generalizations extending beyond the study *sample*, are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn.

vasoconstriction

Decrease of the calibre of the blood vessels leading to a decreased blood flow.

antonym *vasodilation*

vasodilation

Increase in the calibre of the blood vessels, leading to an increased blood flow.

antonym *vasoconstriction*

vector

See *cloning vector*

vehicle

Substance(s) used to formulate active ingredients for administration or use.

Note: In this context, it is a general term for solvents, suspending agents, etc.

venom

Animal toxin generally used for self-defence or predation and usually delivered by a bite or sting.

ventilation

1. Process of supplying a building or room with fresh air.
2. Process of exchange of air between the ambient atmosphere and the lungs.
3. In physiology, the amount of air inhaled per day.
4. Oxygenation of blood.

ventricular fibrillation

Irregular heartbeat characterized by uncoordinated contractions of the ventricle.

vermicide

Substance intended to kill worms.

vermifuge

Substance that causes the expulsion of intestinal worms.

vertigo

Dizziness; an illusion of movement as if the external world were revolving around an individual or as if the individual were revolving in space.

vesicant

1. adj., Producing blisters on the skin.
2. n., Substance that causes blisters on the skin.

vesicle

1. Small sac or bladder containing fluid.
2. Blisterlike elevation on the skin containing serous fluid.

virtually safe dose, VSD

Human exposure over a lifetime to a carcinogen which has been estimated, using mathematical modelling, to result in a very low incidence of cancer, somewhere between zero and a specified incidence, e.g. one cancer in a million exposed people.

virucide

Substance used to control viruses.

[5]

Synonym antiviral

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.

volatile organic chemicals, VOC

Any organic compound having, at 293.15 K, a vapor pressure of 0.01 kPa or more, or having a corresponding volatility under the particular condition of use.

[17]

waste

Anything that is discarded deliberately or otherwise disposed of on the assumption that it is of no further use to the primary user.

wasting syndrome

Disease marked by weight loss and atrophy of muscular and other connective tissues that is not directly related to a decrease in food and water consumption.

Weibull model

Dose-response model of the form

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

where $P(d)$ is the probability of a tumour (or other response) from lifetime, continuous exposure at dose d until age t (when tumour is fatal), α is a fitted dose parameter (sometimes called the Weibull parameter), β is a fitted dose parameter, and γ is the background response rate.

weight-of-evidence for toxicity

Extent to which the available biomedical data support the hypothesis that a substance causes a defined *toxic* effect such as cancer in humans.

withdrawal effect

Adverse event following withdrawal from a person or animal of a *drug* to which they have been chronically *exposed* or on which they have become dependent.

working zone

Space measuring up to 2 m over the level of the floor or platform that contains a worker's permanent or temporary station.

x-disease

Hyperkeratotic disease in cattle following *exposure* to chlorinated dibenzo-p-dioxins, naphthalenes and related compounds.

xenobiotic

Compound with a chemical structure foreign to a given organism.

Note: The term is frequently restricted to manmade compounds.

yeast two-hybrid system

Genetic method for analysing the interactions of proteins.

zero order kinetics

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

[2]

zoocide

Substance intended to kill animals.

zygote

1. Cell such as a fertilized egg resulting from the fusion of two *gametes*.
2. Cell obtained as a result of complete or partial fusion of cells produced by *meiosis*.

DRAFT Provisional Recommendations

ANNEX 1

ABBREVIATIONS AND ACRONYMS USED IN TOXICOLOGY

ADI	Acceptable daily intake
ADME	Absorption, distribution, metabolism, excretion
AF	Assessment factor
AIC	Akaike Information Criteria: a statistical procedure that provides a measure of the goodness-of-fit of a dose-response model to a set of data. $AIC = -2 \times (LL - p)$, where LL is the log-likelihood at the maximum likelihood fit, and p is the degrees of freedom of the model (usually, the number of parameters estimated).
ALARA(P)	As low as reasonably achievable (practicable) In UK regulations relating to worker exposure In USA goal of risk management (USNRC regulations)
ATP	Adenosine triphosphate
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
BMC	Benchmark concentration
BMCL	Confidence limit for BMC
BMD	Benchmark dose
BMDL	Confidence limit for BMD
BMDS	Benchmark dose at a given standard deviation
BMR	Benchmark rate
BOD	Biochemical oxygen demand

b.w.	Body weight
CMR	Carcinogenic, mutagenic and reproductive (toxicant)
CoMFA	Comparative molecular field analysis
CSAF	Chemical specific adjustment factor
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 n % of a population
EDI	Estimated daily intake
ED _n	Median effective dose to n % of a population
EEC	Estimated exposure concentration or Expected exposure concentration
EED	Estimated exposure dose
EEL	Environmental exposure level
EMDI	Estimated maximum daily intake
EQS	Environmental quality standard
ETS	Environmental tobacco smoke
GLP	Good laboratory practice
GFR	Glomerular filtration rate
GMO	Genetically modified organism
HAL	Health advisory level
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
LEDx	Lowest effective dose for a biological effect in x% of the individuals in the test population
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
MAK	Maximale arbeitsplatz konzentration (German)
MEL	Maximum exposure limit
MF	Modifying factor
MFO	Mixed function oxidase
MOE	Margin of exposure
MPC	Maximum permissible concentration
MRL	Maximum residue limit
MRL	Minimal risk level (ATSDR)
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)
NAG	<i>N</i> -acetyl-D-glycosaminidase
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
OR	Odds ratio
PADI	Pseudo-acceptable daily intake

PBPK	Physiologically-based pharmacokinetic modelling
PBPD	Physiologically based pharmacodynamic modelling
PBTK	Physiologically based toxicokinetic modelling
PEL	Permissible exposure limit
PBT	Persistent, bio-accumulative and toxic
p.c.	Per cutim (Latin) = Through the skin
PEL	Permissible exposure limit
PIPs	Persistent inorganic pollutants
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.o.	Per os (Latin) = By mouth
POPs	Persistent organic pollutants
<i>P_{ow}</i>	Octanol water partition coefficient
Q	Quality factor (radiation)
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
REL	Recommended exposure limit (NIOSH)
RfC	Reference concentration

RfD	Reference dose
RNA	Ribonucleic acid
RNS	Reactive nitrogen species
RR	Rate ratio; relative risk
ROS	Reactive oxygen species
SAR	Structure-activity relationship, Standard absorption rate
s.c.	Subcutaneous
SCE	Sister chromatid exchange
SD	Standard deviation
SE	Standard error
SMR	Standard mortality ratio, 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-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
TTC	Threshold of toxicological concern

TWA	Time-weighted average
TWAC	Time-weighted average concentration
TWAE	Time-weighted average exposure
TWI	Tolerable weekly intake
UDP	Uridine diphosphate
UF	Uncertainty factor
V_{\max}	Maximum velocity
vPvB	Very persistent and very bio-accumulative
VSD	Virtually safe dose

ICPAC Provisional Recommendations

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
DFG	Deutsche Forschungsgemeinschaft (German Research Council)
EC	European Community, European Commission
EAC	European Agency for Chemicals
ECB	European Chemicals Bureau
EDC	Endocrine Disrupting Compound
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
EU	European Union
EUROTOX	European Society of Toxicology
EUSES	European Uniform System for Evaluation of Substances
FAO	Food and Agricultural Organization
FDA	Food and Drug Administration (USA)
FIOH	Finnish Institute of Occupational Health
IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
ICCA	International Council of Chemical Associations
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
ISEAAA	International Society for Exposure Assessment and Analysis
ISO	International Organization for Standardization
IUCLID	International Uniform Chemical Information Database - containing unvalidated property and hazard information for 2,604 EU high production

volume chemicals, submitted under the Existing Substances Regulation, EC 793/93.

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
NAS	National Academy of Sciences
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
OEHHA	Organization of Environmental Health Hazard Assessment (USA)
OMS	Organisation Mondiale de la Santé, same as WHO
OSHA	Occupational Safety and Health Administration (USA)
PIC	Prior Informed Consent
REACH	Registration, Evaluation and Authorisation of Chemicals
RIVM	Rijksinstituut voor Volksgezondheid en Milieu
RSC	Royal Society of Chemistry
SCOPE	Scientific Committee on Problems of the Environment (ICSU)
SOT	Society of Toxicology (USA)
TOSCA	Toxic Substances Control Act (USA)
UNEP	United Nations Environment Programme

USEPA United States Environmental Protection Agency, same as EPA
USFDA United States Food and Drug Agency
WHO World Health Organization, same as OMS

IUPAC Provisional Recommendations

ANNEX 1.

CLASSIFICATION OF CARCINOGENICITY

1. Classification according to IARC [12]

Classification based on the weight of the evidence and not on *potency* as follows.

1. Sufficient evidence. Causal relationship has been established between *exposure* to the agent and human cancer: a positive relationship has been observed between exposure to the agent and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence.

2. Limited evidence. Positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

3. Inadequate evidence. Available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association.

4. Evidence suggesting lack of carcinogenicity. There are several adequate studies covering the full range of doses to which human beings are known to be *exposed*, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. A conclusion of "evidence suggesting lack of *carcinogenicity*" is inevitably limited to the cancer sites, circumstances and doses of exposure and length of observation covered by the available studies. In addition, the possibility of a very small *risk* at the levels of exposure studied can never be excluded.

5. Overall evaluation. Total body of evidence is taken into account; the agent is described according to the wording of one of the following categories, and the designated group is given. The categorization of an agent is a matter of scientific judgement, reflecting the strength of the evidence derived from studies in humans and in experimental animals and from other relevant data.

Group 1 The agent (mixture) is carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.

This category is used only when there is sufficient evidence of carcinogenicity in humans.

Exceptionally, an agent (mixture) may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent (mixture) acts through a relevant mechanism of carcinogenicity.

Group 2 This category includes agents, mixtures and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of

carcinogenicity in experimental animals. Agents, mixtures and exposure circumstances are assigned to either 2A (probably carcinogenic to humans) or 2B (possibly carcinogenic to humans) on the basis of epidemiological and experimental evidence of carcinogenicity and other relevant data.

Group 2A The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans

This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that operates in humans. Exceptionally, an agent, mixture or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.

Group 2B The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans

This category is generally used for agents, mixtures and exposure circumstances for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is inadequate evidence of carcinogenicity in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

Group 3 The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.

This category is used most commonly for agents, mixtures and exposure circumstances for which the *evidence of carcinogenicity is inadequate* in humans and *inadequate or limited* in experimental animals. Exceptionally, agents (mixtures) for which the *evidence of carcinogenicity is inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents, mixtures and exposure circumstances that do not fall into any other group are also placed in this category.

Group 4 The agent(mixture) is probably not carcinogenic to humans.

This category is used for agents or mixtures for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals. In some circumstances, agents or mixtures for which there is inadequate evidence of carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly supported by a broad range of other relevant data, may be classified in this group.

3. Classification according to the USEPA [13, 14]

Group A: "Human Carcinogen"

"This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer."

Group B (1 and 2): "Probable Human Carcinogen"

"This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient". The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiological studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient evidence of carcinogenicity" in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate evidence" or "no data" from epidemiologic studies would usually be categorized under Group B2."

Group C: "Possible Human Carcinogen"

"This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate."

Group D: "Not Classifiable as to Human Carcinogenicity"

"This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available."

Group E: "Evidence of Non-Carcinogenicity for Humans"

"This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies."

The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances."

3. Classification according to the European Union [15]

For the purpose of classification and labelling and having regard to the current state of knowledge, such substances are divided into three categories:

Category 1

Substances known to be carcinogenic to man. There is sufficient evidence to establish a casual association between human exposure to a substance and the development of cancer.

Category 2

Substances which should be regarded as if they are carcinogenic to man. There is sufficient evidence to provide a strong presumption that human exposure to a substance may result in the development of cancer, generally on the basis of:

- appropriate long-term animal studies,
- other relevant information.

Category 3

Substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies, but this is insufficient to place the substance in category 2

4. Classification according to the American Conference of Governmental Industrial Hygienists, Inc. (ACGIH) [16]

A1: Chemical substances that are confirmed to be carcinogenic for humans

A2: Chemical substances that are suspected to be carcinogenic for humans

A3: Chemical substances that are carcinogenic for animals

A4: Substances that are not classified as carcinogenic

A5: Substances that are not suspected to be carcinogenic for humans

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IUPAC Provisional Recommendations