

Comprehensive Glossary of Terms Used in Toxicology

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Preface

This book represents a culmination, or at least a resting point, in the long-term project that has resulted in five glossaries published as IUPAC Recommendations in Pure and Applied Chemistry.^{1–5} The project was initiated in 1989 by the IUPAC Commission on Toxicology to provide a glossary of definitions of terms used in toxicology. The impetus was the recognition that toxic substances (indeed all substances) are “chemicals”, and that there is a need for chemists to understand the mechanisms of toxicity of the substances with which they deal. Both industrial and academic research chemists are faced with an ever-increasing burden in ensuring a safe environment. Even those who may not be trained as chemists must use chemical and toxicological principles in formulating and enforcing the current legislation introduced to ensure safe handling of substances throughout their life cycle. Thus, there is a need for an unambiguous vocabulary of terms, both for specialist interpretation of the relevant literature and for warning about hazard and risk that must be controlled and eliminated or minimized.

The starting point of the project was a general glossary of terms in toxicology that collected relevant terms from a variety of sources and revised many of them, with contributions from specialists covering the wide range of knowledge required. IUPAC specialists in terminology advised on details of presentation of terms and definitions. The resultant glossary was submitted to Pure and Applied Chemistry for publication following the normal refereeing process for an IUPAC Recommendation.⁶ This procedure has been the foundation for future glossary development.

The original glossary was followed by a glossary of terms in toxicokinetics.⁷ These two glossaries were later combined and revised,¹ taking into account more recent developments in toxicological science and regulatory activity. Thereafter, it became clear that there were gaps in coverage of terms related to specialized aspects of toxicology that were becoming increasingly important in their own right. These areas of toxicology were covered in new IUPAC glossaries of terms used in ecotoxicology,² immunotoxicology,² neurotoxicology,⁴ and reproductive toxicology and teratology.⁵ This book consolidates all these documents, and expands their contents with the addition of terms that have been newly introduced in toxicology or whose absence in the previous publications we felt should be addressed. We have taken the opportunity to harmonize definitions between the various sub-disciplines of toxicology, and to correct a few errors and oversights in our earlier work. Retrospection has also resulted in a uniform syntax and formatting for the construction and presentation of

definitions that we believe is an improvement on that used in the earlier glossaries; we hope that the current document will thus contribute to the continuing development of the IUPAC standard for such documents.

In a compilation of terms that intends to be anything short of a complete word list of the language, decisions of inclusion and exclusion must be made. The vocabulary of toxicology necessarily overlaps with those of medicine, physiology, biochemistry and ecology, to name a few, and this takes us on occasion into the more specialized realms of cognate disciplines such as anatomy, histology, immunology, neuroscience, molecular biology, epidemiology and population biology. We have also included a number of terms in regulatory toxicology and jurisdictional matters relating to harmful substances. In each case, where we have drawn the line on inclusion reflects our personal preferences, based on decisions about what we think will be a reasonable collection of terms, hoping both to achieve internal consistency and to meet the needs of most readers who may consult the glossary as they explore the relevant toxicological literature. Our aim has been to provide a one-stop glossary of terms commonly used in toxicology so that chemists reading the toxicological literature will not often need to consult secondary sources in order to understand terms with which they are unfamiliar.

All headwords are listed in the singular, in bold type, with the definition following in plain text. When the plural may be a nonstandard form, it is listed and designated (pl), e.g., “**meninx/meninges** (pl)”. When the form of speech may be unclear it is specified as (n), (v) or (adj) after the headword, and when more than one form of speech is indicated, the definition is written so as to apply to the first part of speech listed. When a definition includes a term that is itself another defined term in the glossary, the term is italicized for cross-referencing, but only at first use in the individual entry. However, we realize that complete cross-referencing in this manner is nearly impossible to achieve – nor is it desirable, as italicizing too many general terms in a definition detracts from its readability, and here judgment has been exercised. Italicizing of individual words does not always mean they combine to form a defined term. For instance, under “**optimal stress response**”, *somatic growth rate* appears in italics. This grouping does not itself occur as a headword, but rather the three words ‘somatic’, ‘growth’, and ‘rate’ are defined individually, and would be consulted in sequence for a full explanation of the term. Because Latin names of biological species are italicized by convention, they are additionally in bold here to avoid confusion with cross-referencing.

Notes are included for many terms; these are not intended to be encyclopedic, but rather to provide clarification or remove ambiguity when a strict definition may not be entirely clear. Notes are also used to indicate when a term may be in common use but its use is to be discouraged (e.g., “heavy metal”). In general, commonly preferred or American spelling has been adopted for the main entry terms; thus, for example, anesthetic (not anaesthetic), neuron (not neurone), disc (not disk), and tumor (not tumour). Further, somewhat arbitrary decisions have necessarily been made in listing alternative forms of terms as the headword (e.g., vasospasm instead of angiospasm, β -blocker instead of β -antagonist, and intervertebral disc instead of spinal disc). We have generally tried to use the form we consider to be in most common usage, and to cross-reference the less-used term if it seems also to be common; but, if a desired entry is not found under one construction, it may have to be sought under another.

We attempt to give a correct IUPAC name for all chemical structures mentioned, and the manuscript has been passed by the IUPAC Interdivisional Committee on Terminology, Nomenclature and Symbols (ICTNS). This, too, can become a daunting task when particularly lengthy names for complex natural products or pharmaceuticals are involved. And, in some cases different ‘correct’ IUPAC conventions may lead to alternative names, with the Preferred IUPAC Name (PIN) not always available in the literature. When a drug name is given as the International Non-proprietary Name, it is indicated as such by ‘(INN)’. Enzyme Commission (EC) numbers are provided for enzymes.

In existing glossaries, dictionaries, or other compilations of words, compound or multi-word terms are often listed consistently under the final word (*e.g.*, “compound term: See term, compound”) without regard to what component of the term the user may be most likely to be searching. Here, we do so judiciously. For instance, we suppose it is helpful to list various antibodies (anti-idiotypic, blocking, cross-reacting, enhancing, ...) or mazes (Barnes, Biel water, elevated plus, radial arm, ...) together under “antibody” or “maze”, respectively. But we have decided the same is not true of various “models”, and “biotic ligand model”, “biphasic dose-effect model”, “conceptual site model” and “two-compartment model” are alphabetized as written here. In most cases we have included cross-referencing for compound terms to the form associated with the definition. Our decisions are necessarily somewhat arbitrary, and may not suit the needs of all users. We can’t give specific guidance in these cases, but suggest that for such multi-word terms, the reader should consider possible variants.

A note on sources: All definitions taken from the earlier sources^{1–5} are indicated as [ref. 1], [ref. 2], *etc.* Modifications are designated as “[After ref. X]”, and new terms or those substantially modified from our previous glossaries are designated “[*]”. Several of the approximately 5,000 definitions are taken from the IUPAC Gold Book⁸ on chemical terminology, and are designated as “[ref. 8]”. When a definition is cited as being from any of [ref. 1–5], the reader may look to that publication to see whether it originated there, or is attributed to, or modified from, an earlier source. All references (1–8) are currently open access online.

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A large number of reviewers, some identified and some anonymous, have made invaluable contributions to the development of this work, and many (when known) have been acknowledged in the individual documents.^{1–7} Early encouragement was provided by successive Chairs of the IUPAC Commission on Toxicology (COMTOX), Profs. Philippe Grandjean and Rita Cornelis, and their support has continued throughout the years. The meticulous work of Dr. Karl-Heinz Hellwich in reviewing all the nomenclature was invaluable. We would particularly like to single out our coauthors on the foundation publications, Profs. Monica Nordberg,^{1,2} Ole Andersen² and Reinhild Klein.³

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Alphabetical List of Terms

ABC transporter

See *transporter, ABC*.

ABL oncogene

See *oncogene, ABL*.

ABO blood group system

See *blood group system, ABO*.

Ad4BP

See *adrenal 4 binding protein*.

A/D ratio

Ratio of the *adult toxic dose* to the developmentally toxic dose.

[ref. 5]

AMPA receptor

See *receptor, 2-amino-3-(3-hydroxy-5-methyl-1,2-oxazol-4-yl)propanoic acid (AMPA)*.

ANCA-associated vasculitis

See *vasculitis, antineutrophil cytoplasmic autoantibody-associated vasculitis*.

APECED syndrome

See *polyendocrinopathy, autoimmune*.

ATP

See *adenosine triphosphate*.

abdomen (n)/abdominal (adj)

1. Part of the body between the *thorax* and the pelvis in *vertebrates*.
2. Most posterior segment of the insect body.

[*]

abdominal cavity

See *cavity, abdominal*.

abiological

See *abiotic*.

abiotic

abiological

Opposite term: *biotic*.

Not associated with living organisms.

[ref. 1]

abiotic degradation

See *degradation, abiotic*.

abiotic transformation

See *transformation, abiotic*.

ablepharia (n)/ablepharous (adj)

Congenital absence of the eyelids.

[ref. 5]

abortifacient

Substance that causes *pregnancy* to end prematurely and causes an *abortion*.

[ref. 1]

abortion, induced

Intentional termination of a *pregnancy* with death of the *embryo* or *fetus*.

[ref. 5]

abortion, spontaneous

miscarriage

Unintentional termination of *pregnancy* before the *embryo* or *fetus* has developed to the stage of independent *viability*, or in humans before the 20th week of *gestation*.

[ref. 5]

absolute bioavailability

See *bioavailability, absolute*.

absolute fitness

See *fitness*.

absolute lethal concentration (LC₁₀₀)

See *lethal concentration, absolute*

absolute lethal dose (LD₁₀₀)

See *lethal dose, absolute*.

absolute risk

See *risk, absolute*.

absorbance (A)

Logarithm of the ratio of incident to transmitted *radiant power* through a sample (excluding the effects of sample cell walls).

Note 1: Depending on the base of the logarithm, decadic and Napierian absorbances are used. Symbols: A , A_{10} , A_e .

Note 2: Absorbance is sometimes called extinction, although the term “extinction”, better called *attenuance*, is reserved for the quantity that takes into account the effects of luminescence and scattering as well.

Note 3: When natural logarithms are used, the Napierian absorbance is the logarithm to the base e of the incident *spectral radiant power*, essentially monochromatic, divided by the transmitted spectral radiant power, P_λ .

[ref. 1]

absorbate

Substance that enters and is retained inside a solid or semisolid *matrix* (*absorbent*).
[ref. 2]

absorbed dose (of a substance)

See *dose*, *absorbed*.

absorbed dose (of ionizing radiation)

Energy imparted by *ionizing radiation* to a specified volume of matter divided by the mass of that volume.
[ref. 1]

absorbent

Solid or semisolid *matrix* that is able to accommodate and retain an *absorbate*.
[ref. 2]
See also *sorbate*; *sorbent*.

absorptance (in chemistry), α

Absorbed radiant power divided by the incident radiant power. Also called *absorption factor*. When $\alpha \leq 1$, $\alpha \approx A_e$, where A_e is the Napierian absorbance.
[ref. 1]
See also *absorbance*.

absorption (general)

1. Process of one material (*absorbate*) being retained by another (*absorbent*).
Note: Absorption may be the physical solution of a gas, liquid, or solid in a liquid, attachment of molecules of a gas, vapor, liquid, or dissolved substance to a solid surface by physical forces, *etc.*
2. Transfer of some or all of the energy of radiation to matter that 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 *chemical species*.

[ref. 2]
See also *adsorption*; *sorption*.

absorption (in biology)
uptake

Penetration of a substance into an organism and its cells by various processes, some specialized, some involving expenditure of energy (*active transport*), some involving a *carrier* system, and others involving passive movement down an electrochemical gradient (*passive transport*).
Note: In mammals, absorption is usually through the respiratory tract, *gastrointestinal tract*, or skin into the circulatory system and from the circulation into *organs*, *tissues*, and *cells*.

[ref. 2]

absorption (of radiation)

Phenomenon in which radiation transfers some or all of its energy to matter that it traverses.
[ref. 1]

absorption, systemic

Uptake to the blood and transport via the blood of a substance to one or more organs or *compartments* in the body distant from the site of *absorption*.

[ref. 2]

absorption coefficient (in biology)

absorption factor

Absorbed quantity (*uptake*) of a substance divided by 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.

[ref. 1]

absorption factor

See *absorptance* (in chemistry); *absorption coefficient* (in biology).

abundance

1. Total number of individual organisms in a *population*, seen over a defined period of time in a certain place.

Note: For abundance of fish, an estimate of total weight may replace number.

2. Total number of organisms per unit of *habitat* space seen over a defined period.
3. Amount of an element that exists in nature, usually expressed in relative terms as a percentage of the total amount of all elements in a given medium (*e.g.*, the Earth's crust).
4. Amount of an isotope of an element that exists in nature, usually expressed in relative terms as a percentage of the total amount of all isotopes of the element.

[ref. 2]

abundant element

See *element*, *abundant*.

abundant metal

See *element*, *abundant*.

abuse (of substances)

Improper use of *drugs*, solvents or other substances.

[ref. 1]

abzyme

Antibody or antibody construct with catalytic activity.

[ref. 3]

acaricide

Substance intended to kill mites, ticks, or other *Acaridae*.

[ref. 1]

acceptable daily intake

See *daily intake*, *acceptable*.

acceptable daily intake (ADI) not allocated

See *no-acceptable-daily-intake-allocated*.

acceptable daily intake, temporary

Value for the *acceptable daily intake* (ADI) 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 (see *uncertainty 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.

[ref. 1]

acceptable residue level of an antibiotic

See *residue level of an antibiotic, acceptable*.

acceptable risk

See *risk, acceptable*.

accepted risk

See *risk, accepted*.

accessible

Capable of being entered or reached; easy of access; such as one can go to, come into the presence of, reach, or lay hold of.

[ref. 2]

accessibility

See *bioaccessibility*.

accessory cell

Cell that assists in the *adaptive immune response* but does not directly mediate specific *antigen* recognition.

Note 1: Accessory cells include *phagocytes, mast cells, dendritic cells, and natural killer cells*.

Note 2: The term accessory cell is often used to describe *antigen-presenting cells*.

[ref. 3]

accessory molecule

Molecule other than *immunoglobulin, T-cell receptor, or major histocompatibility complex molecule* that participates in *T-lymphocyte* recognition and response to *antigen*.

[ref. 3]

accessory rib

Rib arising from a cervical *vertebra (cervical rib)*, or *supernumerary* rib arising from a *thoracic* or lumbar vertebra.

[ref. 5]

accessory sex gland

Any gland, other than a *gonad*, associated with the genital tract, such as the *bulbourethral* gland and *prostate*.

[ref. 5]

accessory sex organ

secondary sex organ

Organ or structure other than the *gonads* that matures at *puberty* and assists indirectly in *sexual reproduction* by nurturing and transporting *gametes*.

Note 1: In the human female the accessory sex organs include the *Fallopian tubes*, *uterus*, *vagina*, and the external genitalia.

Note 2: In the human male, the accessory sex organs include the *epididymis*, *vas deferens*, *ejaculatory duct*, *urethra*, *seminal vesicles*, *bulbourethral glands*, *prostate*, and *penis*.

[ref. 5]

accidental cell death

Death of a cell by a catastrophic process such as acute physical, mechanical, chemical or osmotic injury, in contrast to *programmed cell death*.

[*]

accidental exposure

See *exposure*, *accidental*.

acclimation (n)/acclimate (v)

acclimatization (n)/acclimatize (v)

biological acclimatization

1. Modification or adjustment of a biological process or structure that helps to maintain *homeostasis* in response to a change in environment.

Note: The modification occurring in acclimation may be physiological, in response to changes in the physical environment (*e.g.*, thermoregulation), including changes in the concentration of a *toxicant*. It may also refer to behavioral changes reflecting psychological adjustment.

2. Processes, including selection and *adaptation*, by which a *population* of microorganisms develops a *tolerance* to a substance that may follow acquisition of the ability to degrade the substance.
3. Experimental manoeuvre of allowing an organism to adjust to its environment prior to undertaking a *study*.

[*]

acclimatization, biological

See *acclimation*.

accumulation (in biology)

See *bioaccumulation*.

accumulation factor (AF)

See *biota-sediment accumulation factor*.

See also *bioaccumulation factor*.

accuracy

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

[ref. 1]

acetylcholine (ACh)

2-acetoxy-*N,N,N*-trimethylethanaminium

2-(acetyloxy)-*N,N,N*-trimethylethan-1-aminium (PIN)

Substance that functions as a *neurotransmitter* between *nerve cells* and between nerves and muscles.

[ref. 4]

acetylcholine receptor

See *receptor, acetylcholine*.

acetylcholinesterase (AChE)

acetylcholine hydrolase

Enzyme (EC 3.1.1.7) that hydrolyzes *acetylcholine*.

[ref. 4]

acetylcholinesterase inhibitor

Substance that inhibits the action of acetylcholinesterase (EC 3.1.1.7) and related enzymes that catalyze the hydrolysis of choline esters, causing hyperactivity in *parasympathetic* nerves.

Note: Examples include *organophosphate* and carbamate *pesticides*.

[*]

 β -N-acetylhexosaminidase

Hydrolytic enzyme (EC 3.2.1.52) that acts on *ganglioside* G_{M2}, producing *N*-acetyl-D-galactosamine and ganglioside G_{M3}.

Note: Deficiency of β -N-acetylhexosaminidase is associated with *Tay-Sachs disease*.

[ref. 5]

acetyltransferase

acyltransferase

Any of a group of enzymes (EC 2.3.x.y) that transfers an acyl group from a donor (*e.g.*, acetyl-coenzyme A) usually to a hydroxyl or amino (aminoacyltransferase) group of a substrate.

Note: Acetylation of xenobiotics is classified as a *phase II biotransformation* reaction.

[*]

achondroplasia (n)/achondroplastic (adj)

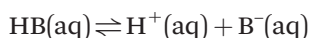
Inherited *disorder* where *ossification* of cartilage is retarded, especially affecting growth of long bones, resulting in very short limbs and a comparatively large head. Type of dwarfism.

Note: Achondroplasia results from a *mutation* in the *fibroblast growth factor receptor* FGFR3 gene, increasing its activity in suppressing *endochondral ossification*.

[ref. 5]

acid dissociation constant, K_a

Equilibrium constant for the following reaction of an acid, HB:



$$K_a = [\text{H}^+][\text{B}^-] / [\text{HB}]c^\circ$$

where $c^\circ = 1 \text{ mol dm}^{-3}$ is the standard amount concentration and activity coefficients have been neglected.

Note 1: The acid dissociation constant, because activity coefficients are neglected, is valid at a specified ionic strength. The thermodynamic dissociation constant is found by suitable extrapolation of the conditional constant to zero ionic strength. Note that it is defined as a dimensionless quantity, but sometimes it is given dimensions by omitting the standard amount concentration.

Note 2: Because the acid dissociation constant differs for each acid, and varies over many degrees of magnitude, the acidity constant is often represented by the additive inverse of its common logarithm, represented by the symbol $\text{p}K_a$ (using the same mathematical relationship as $[\text{H}^+]$ is to pH), viz.:

$$\text{p}K_a = -\log_{10} K_a$$

Note 3: In general, a larger value of K_a (or a smaller value of $\text{p}K_a$) indicates a stronger acid, since the extent of dissociation is larger at the same concentration. [ref. 8]

acid precipitation

Rain, fog, snow, sleet, or other particulate matter from the atmosphere with a pH below 5.6 deposited from the air.

Note 1: Rain under clean air conditions has a pH slightly under 6, caused by dissolved carbon dioxide dissociating to form carbonate and hydrogencarbonate ions. "Acid rain" has a pH of about pH 4.2 to 4.4.

Note 2: Acid precipitation is partly due to volcanic emissions, but, more importantly, results from human activities, such as incineration of sulfur-containing fossils (emission of SO_2) and emission of nitrogen-oxides (NO_x) that are formed in combustion engines.

Note 3: Acid precipitations may fall at a distance remote from emission sources owing to atmospheric transport.

Note 4: Acid precipitation causes acidification of soils and surface waters, with adverse effects on ecosystems.

[After ref. 2]

acid rain

Subtype of *acid precipitation*.

[ref. 2]

acid-volatile sulfide (AVS)

Soil- and *sediment-*associated solid-phase sulfide extractable with cold hydrochloric acid.

Note: AVS may be chemically *available* by acid extraction without being *bioavailable*. Thus, AVS can decrease metal *toxicity* by binding metals in anoxic soils or sediments, thereby rendering them unavailable to most living organisms.

[ref. 2]

acidosis

Opposite term: *alkalosis*

Abnormal increase in hydronium ion activity (decrease in pH below the reference interval measured in the arterial blood) usually caused either by an accumulation of carbon dioxide or acidic metabolites, or by a depletion of alkaline reserve (*i.e.*, bicarbonate).

Note 1: In humans, the blood pH is tightly regulated within a range of 7.35 to 7.45.

Note 2: Acidosis may occur as a result of accumulation of ketones in uncontrolled *diabetes mellitus* (diabetic acidosis) or after calory deprivation (starvation acidosis), or with accumulation of keto-acids at the expense of bicarbonate (*metabolic* acidosis). Suppression of respiration can produce a respiratory acidosis.

Note 3: Some intoxications can produce metabolic and (or) respiratory acidosis.

[ref. 5]

acinus

1. Small sac-like *cavity* in a *gland*, surrounded by secretory cells.
2. Terminal region of the airways of the lung where gas exchange occurs.

[ref. 5]

acoustic meatus

Either of two passages in the ear, one leading to the *tympanic* membrane (external acoustic meatus), and one for passage of nerves and blood vessels (internal acoustic meatus).

[ref. 5]

acoustic neuroma

acoustic neurinoma
vestibular Schwannoma

Noncancerous intracranial *tumor* of the eighth *cranial nerve*.

Note 1: An acoustic neuroma arises from the *Schwann cells*.

Note 2: The eighth cranial (vestibulocochlear) nerve is involved in both hearing and balance.

[ref. 4]

acquired immunity

See *immunity, acquired*.

acquired immunodeficiency syndrome (AIDS)

Disease caused by infection with the *human immunodeficiency virus*, assuming clinical relevance when an infected patient has lost most of his/her *CD4+* *T-cells*, so that infections with *opportunistic pathogens* occur.

[ref. 3]

acrania

Rare *congenital disorder* that occurs in the human *fetus* in which the flat bones in the *cranium* are either completely or partially absent.

[ref. 5]

acrocephaly

acrocephalia
oxycephaly

Type of *cephalic disorder* where the top of the skull is pointed or conical due to premature closure of the *coronal suture* plus any other suture.

Note: Acrocephaly should be differentiated from *Crouzon syndrome*, which involves the *maxilla* and *mandible*.

[ref. 5]

acromegaly

acromegalia

Abnormal enlargement of the hands, feet, and face in adults, caused by overproduction of *growth hormone* by the *pituitary gland*.

Note: Overproduction of growth hormone by the pituitary gland in children causes *gigantism*.

[ref. 5]

acroparesthesia

Abnormal feeling of numbness, tingling, or burning of the skin, typically in the extremities.

[ref. 4]

acrosome

Organelle that develops over the anterior half of the head in the *spermatozoon*.

Note: The acrosome is a cap-like structure derived from the *Golgi apparatus*.

[ref. 5]

acrosome reaction

Process that occurs in the *acrosome* of the *sperm* as it contacts the *egg*, leading to structural changes that facilitate fusion.

[ref. 5]

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.

[ref. 1]

action potential

Brief, spike-like *depolarization* associated with the passage of an impulse without decrement along the membrane of a muscle cell or *nerve cell*.

Note 1: An action potential is used for rapid signaling over a distance.

Note 2: Action potentials also occur in many endocrine cells.

[ref. 4]

activated sludge

Product of treatment of industrial *sludge* with microorganisms and aeration, facilitating its *biodegradation*.

[*]

activation (abiotic)

Conversion of a substance to a more biologically active derivative by modification not involving biological catalysis.

Note: Examples of *abiotic* activation could include activation of a *xenobiotic* to a more *toxic* form, activation of a *prodrug* to an active *drug*, and generation of *photochemical smog* from air *pollutants*.

[*]

activation (biotic)

See *bioactivation*.

See also *activation, complement; activation, lymphocyte; activation, neutrophil*.

activation, complement

Cascade of protein cleavages, releasing *cytokines* that start a further amplifying cascade of cleavages. The result is *complement* activation that, in turn, activates *phagocytes* to degrade foreign and damaged cells or substances, and starts *inflammatory* processes that attract more phagocytes and further activate the cell-killing membrane-destroying complex.

[*]

activation, lymphocyte

Sum of the biochemical processes necessary to stimulate a resting *lymphocyte* to become an immune effector cell, requiring *antigen* and co-stimulatory molecules.

[ref. 3]

See also *costimulation; activation, neutrophil*.

activation, metabolic

Formation of one or more chemically *reactive intermediate(s)* as a result of modification of a molecule by the *xenobiotic*-metabolizing enzymes of liver and other organs.

Note 1: Metabolic activation may lead to acute cell damage and recognition of the damaged cell by the *immune system* as *self*.

Note 2: The reactive intermediate in metabolic activation can also act as a *hapten*.

[ref. 3]

activation, neutrophil

Change in morphology and behavior of a *neutrophil* resulting from exposure to a *cytokine, chemokine, cellular ligand*, or soluble factor.

[ref. 3]

See also *activation, lymphocyte*.

activation-induced cell death

Process by which *immune responses* end in the death of most of the responding *lymphocytes*, leaving only a small number of resting *memory cells*.

[ref. 3]

See also *apoptosis*.

active avoidance test

See *avoidance test, active*.

active immunization

See *immunization, active*.

active ingredient

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

[ref. 1]

Compare *inert ingredient*.

active metabolite

See *metabolite, active*.

active systemic anaphylaxis (ASA) test

Test for determining whether a *drug* can cause *anaphylactic reactions* in an animal following *immunization* with the drug.

[ref. 3]

active transport

See *transport, active*.

activin

Growth factor of the transforming growth factor β superfamily, originally identified as a gonadal factor that stimulated secretion of *follicle stimulating hormone*, also involved in many aspects of development including *mesodermal* induction (see *mesenchyme*), *hematopoiesis*, and *neuronal* differentiation.

[ref. 5]

acute

Opposite term: *chronic*.

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

Note 1: 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 to permit appearance of *toxicity* in susceptible organ systems.

Note 2: In aquatic *ecotoxicology*, acute exposure of the test organisms is typically continuous and of four days or less.

2. In clinical medicine, sudden and severe, having a rapid onset.

[ref. 2]

acute effect

See *effect, acute*.

acute exposure

See *exposure, acute*.

acute lymphoblastic (lymphocytic) leukemia (ALL)

See *leukemia, acute lymphoblastic*.

acute myelogenous leukemia (AML)

See *leukemia, acute myelogenous*.

acute-phase protein

One of a group of serum proteins, mostly produced in the liver, which rapidly changes in concentration (some acute-phase proteins increase, some decrease) during the initiation of an *inflammatory response*.
[ref. 3]

acute-phase response (APR)

Physiological response stimulated by *cytokines* including *interleukin-1*, *interleukin-6*, *interferons*, and *tumor necrosis factor*, characterized by increased vascular permeability, fever, and increased levels of proteins (thus called *acute-phase proteins*) such as *C-reactive protein*, occurring within a few hours of initiation.

Note: Infection, *inflammation*, tissue injury, and occasionally *neoplasms* may trigger the APR.
[ref. 3]

acute rejection

See *rejection, acute*.

acute respiratory distress syndrome (ARDS)

Acute lung failure characterized by *alveolar* and interstitial *edema*, perivascular *pulmonary edema*, and *hyalin membrane* formation, resulting from a variety of underlying causes, including inhalational *toxicities*, that result in increased pulmonary vascular *permeability*.
[ref. 3]

acute-to-chronic toxicity ratio (ACR)

Numerical dimensionless quantity by dividing an *acute toxicity* test result (e.g., LC_{50}) by a *chronic toxicity* test result (e.g., *maximum acceptable toxicant concentration*) where both are expressed in the same units (e.g., substance concentration). Ideally, the data are for the same *chemical species*.

Note 1: The ACR is in principle the inverse of an *application factor* and is used in a similar manner, commonly for estimating chronic toxicity of a substance on the basis of its acute toxicity.

Note 2: The ACR should be greater than one because the ratio compares an acute to a chronic value.
[ref. 2]

acute toxicity

See *toxicity, acute*.

acute toxicity test

See *toxicity test, acute*.

acyclicity

Irregular or absent *estrous cycles*.
[ref. 5]
Compare *anestrus*.

adactyly

adactylia
adactylism

Congenital absence of fingers or toes.
[ref. 5]

adaptation

physiological adaptation

Process by which an organism stabilizes its physiological condition after an environmental change.

Note: If adaptation exceeds the *homeostatic* range, it becomes pathological and results in symptoms of *disease* (*adverse effects*).

[After ref. 1]

adaptation, genetic

Result of random genetic variation due to *mutation* and (or) to changes in *allele* frequencies, causing variation in the survival and reproductive success of individuals and hence of groups of organisms, with the consequence that those best adjusted to their *environment* flourish.

Note: Genetic *adaptation* underlies the concept of *natural selection* leading to Darwinian *evolution*.

[ref. 2]

adaptive immune response

See *immune response, adaptive*.

adaptive immune system

That part of the *immune* system responsible for the *adaptive immune response*.

[ref. 3]

adaptive response

See *response, adaptive*.

added risk

See *risk, added*.

addiction

Compulsive, uncontrolled reward-seeking behavior, especially referring to substance *abuse*.

Note: An addiction may be psychological, referring to a craving or felt need for a behavior that produces a desired mental state without a known physiological basis, or it may be a physical (physiological) dependence in which discontinued use of a substance leads to symptoms of *withdrawal*.

[ref. 4]

See also *habituation*.

Addison disease (autoimmune)

Adrenocortical hypofunction characterized by *hypotension*, weight loss, *anorexia*, and weakness.

Note 1: The most common form is *idiopathic Addison disease*, mediated by *autoimmune* mechanisms. *Autoantibodies* specific to the adrenal cortex are specific diagnostic markers of this form.

Note 2: *Steroid 21-monooxygenase* (EC 1.14.14.16; 21-hydroxylase), a cytochrome P450 steroidogenic enzyme, is one of the major targets of adrenal autoantibodies in idiopathic Addison disease as well as in Addison disease in the context of autoimmune polyglandular syndromes (*polyendocrinopathies, autoimmune*).

Note 3: Hypofunction or failure of the adrenal gland may also be a manifestation of *antiphospholipid syndrome* due to *thrombosis* of the blood vessels of the adrenal glands.

[ref. 3]

additive effect

See *effect, additive*.

additive index

Quantification of the joint action of *toxicants* in a *mixture* by adding measures of their *toxicity* calculated in relation to the toxicity of a reference toxicant.

[ref. 2]

additivity (in toxicology)

Property of the toxicities of substances whereby the *toxicity* of a *mixture* of the substances reflects the simple sum of the individual *toxicant* effects.

[ref. 2]

See also *effect, additive*.

addressin

Extracellular protein of the venular *endothelium* serving as a *ligand* to a *homing receptor* for *lymphocytes*.

Note: Addressins are *glycoproteins* recognized by *L-selectin*.

[ref. 3]

addressin, vascular

Cell *adhesion molecule* present on the luminal surface of blood and *lymph* vessel endothelium, recognized by *homing* molecules that direct *leukocytes* to tissues with the appropriate “address”.

[ref. 3]

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 change in connectivity, but no loss, of atoms within the moieties A and B.

Note 1: Adduct stoichiometries other than 1:1 are also possible, for example, a bis-adduct (2:1). An “intramolecular adduct” can be formed when A and B are groups contained within the same molecular entity.

Note 2: Adduct is a general term that, whenever appropriate, should be used in preference to the less explicit term “complex”. It is also used specifically for products of an addition reaction.

[ref. 8]

Note 3: In toxicology, adducts of *reactive intermediates* or bioactivated substances to DNA and proteins often cause cell damage.

[*]

adenocarcinoma

Malignant tumor formed from *glandular epithelial* tissue or formed in a glandular pattern.

[ref. 5]

adenoma

Benign *tumor* arising from *epithelial* cells in glandular tissue.

[ref. 4]

adenosine deaminase (ADA) deficiency

Lack of the enzyme adenosine deaminase (EC 3.5.4.4), which catalyzes the deamination of adenosine and deoxyadenosine to produce inosine and deoxyinosine, respectively. Affected individuals have a form of *severe combined immunodeficiency*.

[ref. 3]

adenosine receptor

Any of four types of purinergic *receptors* that respond to the nucleoside adenosine, two of which are involved in release of the *neurotransmitters*, *dopamine* and *glutamate*. Note: The stimulatory effects of caffeine are thought to be due to caffeine's blockade of adenosine receptors.

[ref. 4]

adenosine triphosphate (ATP)

Major molecular component in the energy currency of the *cell*.

Note 1: In *eukaryotes*, ATP is produced mainly in the *mitochondria* through *oxidative phosphorylation* under *aerobic* conditions. *Toxic substances* that interfere with delivery of dioxygen to the cell, *poison* the *electron transport chain*, *uncouple* oxidative phosphorylation from ATP synthesis, or interfere with mitochondrial structure or function, compromise the cell's energy utilization.

Note 2: Under conditions of decreased dioxygen, *glycolysis* can become a secondary, though less efficient, source of ATP.

[*]

adenylate energy charge (AEC)

Index reflecting the balance of energy transfer between catabolic and anabolic processes, calculated from the equation

$$\text{AEC} = ([\text{ATP}] + 1/2[\text{ADP}])/([\text{ATP}] + [\text{ADP}] + [\text{AMP}])$$

where ATP, ADP, and AMP are the substance concentrations of adenosine tri-, di-, and monophosphate, respectively.

[ref. 2]

adermia

Congenital absence of skin.

[ref. 5]

adhesion factor

Substance contributing to selective cell-cell and cell-matrix binding.

[ref. 5]

See also *extracellular matrix*.

adhesion molecule

Molecule belonging mainly to the *immunoglobulins*, *integrin superfamily* (e.g., LFA-1, ICAM-1) or *selectins*, expressed on the cell membrane of various cells including those of the *immune system*.

Note: Interaction of adhesion molecules with each other as *receptor* and corresponding *ligand* facilitates cooperation (cross-talk) of cells, *signal transduction*, and information transfer between cells.

[ref. 3]

aditus

Entrance or opening to some interior space or *cavity*.

[ref. 5]

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 aluminum hydroxide) or a suspension in oil of a dead organism (such as fragments of killed *Mycobacterium*) that increases the response to an *antigen*.

[ref. 3]

See also *Freund's adjuvant*.

adjuvant arthritis

See *arthritis*, *adjuvant*.

administration (of a substance)

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

[ref. 1]

adolescence (n)/adolescent (adj)

Stage of human development beginning with *puberty* and ending with *adulthood*.

[ref. 5]

adoptive transfer

Transfer, by *transplantation* of *immunocompetent* cells, of the capacity to mount an *immune response*.

[ref. 3]

adrenal 4 binding protein (Ad4BP)

Transcription factor that regulates the *expression* of the enzymes of *steroid* synthesis and is expressed primarily in steroidogenic cells.

[ref. 5]

adrenal gland

paranephric gland
suprarenal gland

Either of two small *endocrine glands*, one located above each kidney, consisting of a cortex, which secretes several *steroid hormones*, and a *medulla*, which secretes *adrenaline* and *noradrenaline*.

[ref. 5]

adrenaline

adrenalin

epinephrine (INN)

4-[(1R)-1-hydroxy-2-(methylamino)ethyl]benzene-1,2-diol

Catecholamine hormone secreted by the *adrenal glands* that increases heart rate, breathing rate, blood pressure, and carbohydrate metabolism.

[ref. 5]

See also *noradrenaline*.**adrenergic**

1. Relating to or denoting secretion of and (or) response to *adrenaline*, *noradrenaline* or related substances; in particular referring to *sympathetic* nerve fibers.
2. Relating to or denoting an agent that mimics the activity of *adrenaline*, *noradrenaline* or related substances.

[ref. 4]

Compare *cholinergic*.See also *sympathomimetic*. **α -adrenergic receptor**See *receptor*, *α -adrenergic*. **β -adrenergic antagonist**See *β -blocker*. **β -adrenergic blocking agent**See *β -blocker*. **β -adrenergic receptor**See *receptor*, *β -adrenergic*.**adrenoceptor**See *receptor*, *β -adrenergic*.**adrenocorticotrophic hormone (ACTH)**

Hormone secreted by the *pituitary gland* and stimulating the adrenal cortex (see *adrenal gland*).

[ref. 5]

adrenogenital syndromeSee *congenital adrenal hyperplasia*.**adsorbate**

Molecular species of gas, dissolved substance, or liquid that adheres to or is adsorbed in an extremely thin surface layer of a solid substance.

[ref. 2]

adsorbentCondensed phase at the surface of which *adsorption* may occur.

[ref. 2]

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.

[ref. 1]

See also *absorption; interfacial layer; sorption*.

adsorption factor

Amount of substance adsorbed at the interface of a condensed and a liquid or gaseous phase divided by the total amount of the substance available for *adsorption*.

[ref. 1]

adstringent

See *astringent*.

adult

Person or animal that is fully grown, developed, and sexually mature.

[ref. 5]

adulthood

State of being *adult*.

[ref. 5]

adult respiratory distress syndrome (ARDS)

See *acute respiratory distress syndrome*.

adult stem cell

See *stem cell*.

advanced glycation endproduct (AGE)

Protein or lipid that becomes non-enzymatically and stably *glycosylated*.

Note 1: Circulating protein AGEs bind to cell-surface receptors for AGE (RAGE) present on *endothelial cells, macrophages*, and renal mesangial cells, resulting in increased vascular permeability and *cytokine* production.

Note 2: Important sources of AGEs include reaction with methyl glyoxal (produced nonenzymatically from triose phosphate intermediates of *glycolysis*, glyceraldehyde 3-phosphate and dihydroxyacetone phosphate, especially under hyperglycemic conditions) and glyoxal (produced by *lipid peroxidation*). Both are more potent than glucose in the formation of AGE.

Note 3: Production of AGE and occupancy of RAGE have been strongly implicated in the microvascular *pathology* occurring from hyperglycemia due to *diabetes mellitus*.

[*]

See also *glycosylation; nonenzymatic glycosylation*.

advection (in ecotology)

Process of transport of a substance and its properties (*e.g.*, heat) in air or water solely by bulk motion (in water or air currents).

Note: In open-ocean marine systems, advective transport of chemicals into the water column from *sediments* is small compared with that by *diffusion*. In *estuarine* systems, freshwater rivers, and lakes, advective processes can contribute substantially to system transport.

[After ref. 2]

adverse drug reaction

Harmful or unpleasant reaction following administration of a pharmaceutical product.

[*]

adverse effect

adverse outcome

Change in biochemistry, physiology, growth, development morphology, or behavior of an organism, including the effects of aging, that results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to other environmental influences.

[After ref. 1]

See also *adverse event*.

adverse event

Occurrence that causes an *adverse effect*.

Note: An adverse event in clinical studies is any untoward reaction in a human subject participating in a research project; such an adverse event, which may be a psychological reaction, must be reported to an institutional review board.

[ref. 1]

adverse immunostimulation

Antigen-nonspecific, inappropriate, or unintended activation of a component of the *immune system*.

Note: The distinction from *pseudoallergy* is subtle.

[ref. 3]

adverse outcome

See *adverse effect*.

adverse outcome pathway (AOP)

Ordered sequence of *key events* linking an initiating molecular event to an *adverse effect* in an individual organism, population of organisms or an ecosystem, relevant to a specific *risk assessment*.

Note: The causal links between key events in the AOP are referred to as “key event (KE) relationships”.

[*]

Compare *toxicity pathway*.

aeroallergen

Any airborne particle, such as a pollen grain or spore, that triggers an *allergic* reaction in sensitive individuals.

[ref. 3]

aerobe

Organism that requires dioxygen for respiration and hence for life and growth.

[ref. 1]

aerobic

Opposite term: anaerobic.

Requiring dioxygen.

[ref. 1]

aerodynamic diameter (of a particle)

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

[ref. 1]

aerosol

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

Note 1: Owing to their size, aerosol particles (usually less than 100 μm and greater than 0.01 μm in diameter) have a comparatively small sedimentation 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.

[ref. 1]

aetiology

See *etiology*.

afferent

Opposite term: *efferent*.

Inflowing. Of nerves, those that conduct impulses toward the *central nervous system*.

[ref. 4]

affinity

intrinsic affinity

Strength of binding (affinity constant) between a *receptor* (e.g., one *antigen*-binding site on an *antibody*) and a *ligand* (e.g., *epitope* on an antigen).

[ref. 3]

See also *avidity*.

affinity chromatography

Chromatography in which immobilized *antibody* (or *antigen*) is used to select specific antigen (or antibody) from a mixture. The purified *ligand* is then released by disrupting the antibody-antigen interaction, e.g., by changing the pH.

[ref. 3]

affinity maturation

Increase in *antibody affinity* for an *antigen* observed as the *humoral immune response* progresses.

[ref. 3]

agammaglobulinemia

See *agammaglobulinemia, X-linked*.

agammaglobulinemia, X-linked

Bruton syndrome

X-linked impairment of the ability to produce *mature B-cells*, thus characterized by recurrent infections.

[ref. 3]

aganglionic megacolon, congenital

See *Hirschsprung disease*.

age class

Group of organisms of the same age within a *population*.

[ref. 2]

age composition

Distribution of organisms among the various age classes present in the *population*.
Note: The sum of the number of individuals in all *age classes* equals the population size.

[ref. 2]

age distribution

Composition of a *population* in terms of how its *abundance* is distributed across *age classes*.

[ref. 2]

age sensitivity

Quantitative and qualitative age dependence of susceptibility to an *adverse effect*.

[ref. 1]

age-specific birth rate

age-specific fecundity

age-specific fertility rate

Mean number of offspring born to a female in a specific *age class* in a given year, expressed per 1000 females in that age class.

[ref. 2]

age-specific death rate

age-specific mortality

age-specific number of individuals dying

Mean number of deaths as tabulated for a life table interval or for a specific *age class* in a given year, expressed per 1000 in that interval or age class.

[ref. 2]

age-specific fecundity

See *age-specific birth rate*.

age-specific fertility rate

See *age-specific birth rate*.

age-specific mortality

See *age-specific death rate*.

age-specific number of individuals dying

See *age-specific death rate*.

agenesis

Absence or partial development of an organ or body part observed at *birth*.

[ref. 5]

agglutination (n)/agglutinate (v)

Clumping of particles, such as *erythrocytes* or bacteria, caused by bivalent binding of *antibodies* to *antigens* on the surfaces of adjacent particles.

Note: When the particles that agglutinate are erythrocytes, the phenomenon is called hemagglutination.

[ref. 3]

See also *hemagglutinin*; *prozone effect*.

aggregation chimera

Organism made by combining cells from two *embryos* of different *genotypes*.

[ref. 5]

aggregation error

Error in *Bayesian probability* analysis of model systems resulting from the use of a single set of parameters to represent a collection of distinct entities, such as individuals, in a *population*.

[ref. 2]

aging (of a contaminant)

Decrease in *bioavailability* of a *contaminant* with time.

Note: Generally aging of a contaminant is due to increased *absorption* by solid particles.

[ref. 2]

aging (of acetylcholinesterase)

Property of the complex formed by reaction of *organophosphate* (OP) pesticide with *acetylcholinesterase* whereby the reversible enzyme-OP complex dealkylates to form an irreversibly inhibited *enzyme*.

[ref. 2]

aging, rate-of-living theory of

Idea that the total *metabolic* expenditure of a *genotype* is generally fixed, and longevity depends upon the rate of energy expenditure.

[ref. 2]

agnathia

Congenital absence or partial absence of the lower jaw.

[ref. 5]

See also *macrognathia*; *otocephaly*; *synotia*.

agnosia

Impaired ability to recognize or comprehend the meaning of various sensations, not attributable to faulty sensory input or general intellect.

Note: Generally agnosia involves several sensory forms, such as *auditory (acoustic)*, gustatory, *olfactory*, tactile, and visual agnosias.

[ref. 4]

agonist

Opposite term: *antagonist*.

Substance, naturally occurring or otherwise, that binds to cell *receptors* that normally respond to a naturally occurring substance, and produces an effect similar to the natural substance.