Medicine Safety Glossary

The following definitions are provided as a resource to supplement the information provided in the Medicine Safety Education section of the Pfizer.com Web site; they are not intended as a comprehensive list of medicine safety terminology.

A

ADME/Tox: Studies undertaken to determine the **A**bsorption, **D**istribution, **M**etabolism, **E**xcretion, and **Tox**icology properties of compounds.

Adverse effect: See the glossary entry for **Side effect**.

Adverse event: Any untoward medical occurrence in a patient, clinical investigation subject, or consumer following administration of a medicine. The event need not necessarily have a causal relationship with the treatment or usage. (See also the glossary entry for **Serious adverse event**.)

Adverse Event Reporting System: A database of serious adverse events reported to the U.S. Food and Drug Administration (FDA) that supports the post-approval safety surveillance program for approved medicines.

Aggregate: The whole sum, made up of many parts.

Analogue: A compound that resembles another compound in chemical structure, but is not necessarily identical in composition.

B

Benefit-risk profile: Description or analysis of whether the therapeutic benefits of using a pharmaceutical product outweigh the risks involved. This balance can be different for certain groups of patients or for those with particular coexisting conditions/diseases.

Black-box warning: Warning text placed within a black border at the top of the U.S. Prescribing Information to indicate that the drug carries a risk of a serious, possibly life-threatening adverse event.

Blinded/Blinding: A procedure in which one or more parties to the study are kept unaware of the treatment assignment(s). Single-blind studies usually refer to the patients being unaware, while double-blinding usually refers to patients, investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignments. The intent is to limit the occurrence of conscious and unconscious bias in the conduct and interpretation of a clinical study arising from the influence that the knowledge of treatment may have on the recruitment and allocation of patients, their subsequent care, the attitude of patient to the treatments, the assessment of end points, the handling of withdrawals, the exclusion of data from the analysis, and so on.

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C

Common Technical Document (CTD): A standardized organizational structure and format for medicine approval submissions, as agreed upon through the International Conference on Harmonisation (ICH) process.

Concomitant medication: A medicine taken concurrently with another medicine. This includes not only prescribed medicines, but also homeopathic treatments, herbal treatments, vitamins, and other nonprescription medications.

Confounding: A relationship between the effects of two or more causal factors observed in a set of data, such that it is not possible to separate the contribution of any single causal factor to the observed effects.

Controlled study: A method of conducting a clinical trial in which one group of subjects is given an experimental medicine or treatment, while the second group, known as the control group, is given either a standard treatment for the illness or a placebo (an inactive substance). Results obtained in the two groups are then compared to see if the experimental treatment is more effective than the standard treatment or placebo in treating the condition.

Cumulative: Increasing by successive additions.

D

Data mining: The extraction of useful safety information from large data sets or databases.

Data Safety Monitoring Boards/Data Monitoring Committees: Independent committees that may be established by the sponsor (e.g., a pharmaceutical company) to assess at intervals the progress of a clinical study, the safety data, and the critical efficacy end points, and to recommend to the sponsor whether to continue, modify, or stop a study.

Drug-drug interaction: A modification of the effect of a medicine when administered with another medicine. The effect may be an increase or decrease in the action of either substance, or it may be an adverse effect not normally associated with either medicine.

E

Efficacy: The ability of a medicine or treatment to produce a result. A medicine passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the procedure mandated by the U.S. Food and Drug Administration (FDA), Phase 2 clinical trials gauge efficacy, and Phase 3 trials confirm it.

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

Ethics committee: The standing committee in a medical school, hospital, or other health care facility that is charged with ensuring the safety and well-being of human subjects involved in research. Many different terms are used in various countries (e.g., Ethical Review Committee, Research Ethics Board, or [in the U.S.] Institutional Review Board [IRB]).

EudraVigilance system: A European Union centralized data processing network and management system, established by the European Medicines Agency (EMA) to support the electronic exchange, management, and evaluation of unexpected, serious adverse event (see the glossary definitions for **Unexpected adverse event** and **Serious adverse event**) cases related to all medicines approved in the European Economic Area (EEA).

Expedited report/reporting: Safety reports that require reporting within short timeframes to regulatory authorities (such as the FDA in the U.S. or the EMA in Europe). The specific requirements may vary by regulatory agency, but factors typically include the seriousness of the specific adverse event, whether it would be expected to occur (see the glossary definition for **Unexpected adverse event**), and whether it might be related to an investigational medicine.

G

Genotoxicity: Damaging to DNA cell material, thereby capable of causing gene mutation or cancer.

I

Incidence: The number of instances of illness commencing during a given period in a specified population.

Incremental: Made up of a series of regular consecutive additions.

Induction period: The period required for a specific cause to produce a disease.

Informed consent: A process by which a patient/subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the patient's/subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

Investigator Brochure: A compilation of the clinical and nonclinical data on the investigational medicine(s) that are relevant to the study of the investigational medicine(s) in human subjects.

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L

Label: Information provided about a medicine such as the U.S. Prescribing Information or the Summary of Product Characteristics (SPC).

Large simple trials: Studies in which large numbers of patients are randomly assigned to a treatment and then followed observationally.

Latency period: Delay between exposure to a disease-causing agent and the appearance of signs and symptoms of a disease.

M

Mechanistic study: A study where a medicinal product is being used but the purpose of the study is to investigate the normal functioning of the body, or a disease mechanism, rather than the medicinal product. For example, the medicinal product could be used as a tool to study the patient's disease (e.g., the glucose clamp technique to study a patient's diabetes). Another example would be to use L-NMMA (an analogue of arginine) to inhibit nitric oxide synthesis in healthy volunteers in order to investigate the role of nitric oxide in the stomach's response to food.

MedWatch: A system maintained by the U.S. Food & Drug Administration (FDA) for the voluntary reporting of adverse events, potential and actual medical product errors, and product quality problems associated with the use of FDA-regulated medicines, biologics, devices, and dietary supplements.

Mutagenic: Producing or promoting a mutation, which is an alteration in the genetic material (DNA) of the cell that could cause cancer or a birth defect.

N

Nonclinical studies: See the glossary entry for **Preclinical studies**.

O

Observational study: A study in which health outcomes are assessed in predefined groups of individuals. Patients in the study may receive diagnostic, therapeutic, or other interventions according to usual clinical practice, rather than having specific interventions assigned by the investigator or mandated by the study design.

P

Pharmacodynamics: The study of how a medicine affects the body; of particular interest is the relationship between drug concentration and effect, whether desired or undesired.

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Pharmacogenomics: The application of genome science (genomics) to examine human variability in response to a medicine; the exploration of the ways in which these variations can be used to predict how a patient may react to a medicine from both a safety and efficacy standpoint.

Pharmacokinetics: The processes in a living organism of absorption, distribution, metabolism, and excretion of a medicine or vaccine.

Pharmacovigilance: The science and activities relating to the detection, assessment, understanding and prevention of side effects or any other problem related to a medicine.

Phase 1 studies: Initial studies in humans to assess safety and how a drug is handled by the body; may include healthy participants and/or patients.

Phase 2 studies: Controlled clinical studies in patients to assess safety andto evaluate the effectiveness of the drug in the targeted disease/condition.

Phase 3 studies: Expanded controlled and uncontrolled trials to gather sufficient evidence of safety and effectiveness of a drug to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling (See the glossary entry for **Label**.)

Pivotal studies: Clinical studies (usually Phase 3) that provide the benefit-risk data on which regulatory agencies base their decision about whether to approve a new medicine.

Post-approval studies: A study conducted during the post-approval period, often under the terms of the approval to market the medicine. For example, a postmarketing surveillance study (PMS) is designed to obtain additional safety/efficacy data in approved indications, either in formal clinical studies or in noninterventional studies. A postauthorization safety study (PASS) aims specifically to identify or quantify a safety hazard related to an approved medicine.

Preclinical studies: In pharmaceutical development, testing of a medicine with laboratory or animal studies. The term "preclinical" reflects the fact that the first of these studies are conducted prior to clinical studies in humans. Laboratory and animal studies continue once a compound is undergoing clinical testing, however, and so the term "nonclinical" may also be used to describe these studies.

Prevalence: The number of events (e.g., instances of a given disease or condition) in a given population at a designated time.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a study, including any amendments.

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R

Randomized: A study method in which patients are assigned to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Registry: A system of ongoing registration in which data are collected concerning all cases of a particular disease or other health-relevant condition in a defined population such that the cases can be related to a population base. Examples include cancer registries, birth defect registries, and death registries.

Regulatory agency (also known as **regulatory authority**)**:** Bodies having the power to regulate (e.g., those that review submitted clinical data and those that conduct regulatory inspections).

Risk Evaluation and Mitigation Strategy (REMS): A **risk management** framework established in the U.S. under The Food and Drug Administration Amendment Act of 2007 (FDAAA).

Risk management: The comprehensive and proactive application of scientifically-based methodologies toward identifying, assessing, communicating, and minimizing risks so as to establish and maintain a drug's favorable benefit-risk profile in patients.

Risk Management Plan (RMP): A document, for use in regulatory submissions, designed to proactively identify, characterize, prevent or minimize, and communicate risks relating to a medicine. The RMP contains a Safety Specification; a Pharmacovigilance Plan; an evaluation of the need for risk minimization activities; and, if there is a need for additional (i.e., nonroutine) risk minimization activities, a risk minimization plan.

S

Safety signal: A concern about an excess of adverse events compared to what would be expected to be associated with a product's use that suggests further investigation or monitoring may be warranted. This may or may not lead to the conclusion that the medicine caused the event.

Serious adverse event (SAE): Any untoward medical occurrence that at any dose causes death, constitutes a life-threatening event, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect. Note that "serious" differs from "severe," which describes the intensity of an adverse event. (In clinical studies, it is usual practice to record for all adverse events whether they are mild, moderate, or *severe*, but it is the seriousness (not severity) that serves as a guide for defining regulatory reporting obligations.

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Side effect (also known as **adverse effect** or **adverse reaction**)**:** Any undesired action or effect of a medicine or treatment. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental medicines must be evaluated for both immediate and long-term effects.

Spontaneous adverse event report: An unsolicited report on an approved product received directly from an outside source, such as a health professional or a consumer. Spontaneous reports include both serious and nonserious adverse events.

Statistical analysis plan: A document that contains a more technical and detailed elaboration of the principal features of the analysis described in the protocol (see the glossary entry for **Protocol**), and includes detailed procedures for executing the statistical analysis.

Surveillance: A study (or other approach) designed to obtain additional safety information. Surveillance studies may be formal clinical trials or noninterventional, and are often conducted as a post-approval activity.

T

Toxicity: Having the capability to cause death or injury. May pertain to an adverse event produced by a medicine that is detrimental to the subject's health. The level of toxicity associated with a medicine may vary with the condition for which the medicine is used, as well as the dosage used.

Toxicology: The study of the potential for a substance (e.g., a medicine) to have toxic (i.e., harmful) effects on the body.

U

Unexpected adverse event: An adverse event that is not consistent in nature or severity with the applicable company product information (e.g., the Prescribing Information or Summary of Product Characteristics for an approved medicine or the Investigator Brochure for an experimental medicine). Therefore, unexpected events are sometimes said to be "unlisted" or "unlabeled" (with respect to the product information).

Unlisted adverse event: See the glossary entry for **Unexpected adverse event**.