



## Practical addenda

### Addendum 7: Glossary and abbreviations

The reader will find a few terms in this list that have not been used in the text. They have been added because they are terms which can be found in many other publications on drug safety and/or pharmaco-epidemiology.

**ABSOLUTE RISK** = the risk of a new undesirable event, e.g. an ADE, in a specified (e.g. by exposure) population. It is the sum of the reference risk and the drug-associated risk

**ADE** = Adverse Drug Experience or Event. Any undesirable adverse health experience, occurring in association (= usually during treatment, but it may also appear after stopping) with a medicine in man, is an ADE. The association does not imply a causal relationship. Only if the event, for obvious reasons, cannot be drug related, is it not considered an ADE. Certain definitions also exclude adverse effects seen with an overdose

**ADR** = Adverse Drug Reaction. This abbreviation is not used in this document. It is frequently used, however, in the medical literature where its definitions vary between:

1. the same definition as for an ADE (used by some health authorities);
2. the same definition as for an ADE, but with the additional prerequisite that there should be a suspicion that the drug may have at least contributed to the problem (= definition used by many health authorities);
3. a generally recognized side-effect of a drug

**ADVERSE REACTION** = a reaction that is due to a patient characteristic and that is unexpected as judged from the pharmacological and toxicological properties of the drug

**AMBISPECTIVE STUDY** = (cohort) study design in which a part of the data is collected retrospectively and a part of the data is collected prospectively

**ASCERTAINMENT BIAS** = a relatively common type of selection bias. It can occur when the patients in one of the study groups have had more access to medical care than the patients in the other study group(s) or when the patients in the different study groups have been seen by different physicians who categorise symptoms and diagnoses differently

ATTRIBUTABLE RISK or excess risk = the arithmetic difference between the risk in a treated population (i.e. the absolute risk) and that in an untreated control population (i.e. the reference risk)

ATTRIBUTION = process of deducing the causative role of the suspect drug in the production of an ADE

BARDI = an acronym for Bayesian Adverse Reactions Diagnostic Instrument. It is a technique for differential diagnosis of adverse events that relies upon a mathematical calculation of the probability that each individual event is (not) drug induced

BGA = Bundesgesundheitsamt, i.e. the German health authority

BIAS = an inaccuracy which differs in size or direction between the study groups and which results in a lack of comparability of these groups. Bias should not be confused with confounding; the latter relates to the study population, whereas a bias is a flaw in the study design

CASE-CONTROL STUDY = study that identifies a group of persons with the ADE of interest and a suitable comparison group of people without it. The study compares the two groups and looks for differences in antecedent (drug) exposures

CASE REPORT = a report on a single patient. Within the context of pharmacovigilance, a case report describes a patient who has experienced a certain adverse outcome during or after exposure to a defined drug

CAUSALITY ASSESSMENT = a reasonable estimate of the etiologic relation between the drug and an ADE in a patient using it

CHANNELING = a form of allocation bias, where drugs with similar therapeutic indications are prescribed to prognostically different groups of patients. Often a claimed advantage of a new drug channels it to patients with special pre-existing morbidity; hence the term “channeling”

CIOMS = Council for International Organizations of Medical Sciences, an international council aiming at bringing together specialized international medical associations with research interests in order to facilitate and coordinate their activities and to promote international activities in the field of medical sciences

COHORT STUDY = study in which subsets of a defined population, who vary with respect to exposure to a particular drug, are followed over time. The study generally compares the exposed patients to a suitable control group and looks for differences in their ADE incidence rates

CO-MORBIDITY = presence of more than one disease state at a given time in a patient

COMPASS = Computerized On-line Medicaid Pharmaceutical Analysis and Surveillance System, a very large database of Medicaid recipients from various states in the USA

CONCOMITANT EXPOSURE = state in which a population has exposure to more than one variable during the same observation period

CONFOUNDER = a variable, other than the risk factor and outcome variable under study, that is associated with both the risk (i.e. the prescribing of the drug) and a higher or smaller probability of the outcome (i.e. the adverse effect). To be a confounder, the variable must be unequally distributed among the exposed and the unexposed study subjects. A confounder is a property of the population studied

CONTRIBUTORY CAUSE = a drug that plays a role in the etiology of an adverse event along with other causative factors

COST-BENEFIT ANALYSIS = an analysis which compares the cost of a medical intervention with its benefit. Both costs and benefits are measured in the same monetary unit (e.g. a currency)

COST-EFFECTIVENESS ANALYSIS = an analysis which compares the cost of a medical intervention with its effectiveness. Costs are determined in monetary units (e.g. a currency), while effectiveness is measured independently and expressed in any meaningful unit

CO-VARIANT = condition in which the value of a variable changes in accordance with changes in an associated variable

CROSS-SECTIONAL STUDY = study that examines the relationship between an ADE and other variables of interest as they coexist in a defined population at one point in time

CSM = the UK's governmental Committee on the Safety of Medicines

DDD = Defined Daily Dose, a technical unit of measurement of drug utilization. It is the assumed average dose per day for a particular drug used in its main indication in adults; it is estimated based on the scientific literature and/or proposed by a group of experts

DEAR DOCTOR / PHARMACIST LETTER = letter that is sent by a company to all doctors/pharmacists in order to call their attention to a previously unknown safety issue

DECHALLENGE = withdrawal of a drug from the therapeutic regimen in a patient thought to have suffered a drug-induced ADE

DIAGNOSTIC SUSPICION BIAS = distortion that occurs when knowledge of the subject's prior exposure to a putative cause influences both the intensity and the outcome of the diagnostic process

DRUG UTILIZATION STUDY = study designed to describe and quantify patterns of drug use by specific population groups in a specified clinical or social setting

DSRU = Drug Safety Research Unit, an independent charity in Southampton (UK) headed by Professor W. Inman

DUR = Drug Utilization Review, a type of study that is relatively common in certain countries, including the USA where it is often used in health care institutions

EPS = extrapyramidal signs or symptoms

EVENT MONITORING = system of ADE collection which requires the doctor to report all events whether or not they may be drug-related

EXCESS RISK, *see* “attributable risk”

EXPECTED ADE = an ADE whose nature and severity are described as a possible complication in the current summary of the product’s characteristics (e.g. the company’s Core Data Sheet, or Investigator’s Brochure)

FDA = Food and Drug Administration, the USA regulatory agency responsible for the public’s safety through approval or disapproval of drug and food products

FREQUENCY = general term describing the quantitative occurrence of an ADE, disease or other attribute in a population, during a certain time period

GHC = Group Health Cooperative, a non-profit consumer-directed HMO which supplies health care on a prepayment basis to over 320 000 individuals in western Washington state

HAZARD = an act or phenomenon that poses potential harm to somebody or something. Note that the term “hazard” does not include a reference to the risk that the hazard will actually occur

HMO = Health Maintenance Organization, a prepaid health care delivery system having the potential to create and maintain large computerized databases useful in record linkage studies

ICD = International Classification of Diseases. There are up to 10 revisions of this classification system. In order to be complete, a reference to this system should, therefore, refer to the exact revision used. An example: ICD-9-CM = ICD, 9th clinical revision — Clinical Modification

IDIOSYNCRATIC REACTION = an uncharacteristic response to a drug that is unpredictable, patient-specific, and usually very rare

INCIDENCE = number of new ADEs during a defined time period in a specified population

INCIDENCE RATE = the incidence divided by the number of people in the population at risk during the time period concerned

INDICATOR VARIABLE = variable used as a signal for a larger entity

INDIRECT COSTS = costs that do not stem directly from an adverse event but represent the loss of opportunities to use a valuable resource in alternative ways. They include the cost of morbidity (e.g. time lost from work) or mortality (e.g. premature death leading to removal from the work force)

INDUCTION PERIOD = the time required for a specific drug to initiate pathological changes or induce an ADE

INTANGIBLE COSTS = costs due to pain, suffering and grief

INTERNATIONAL MEDICAL BENEFIT / RISK FOUNDATION = a foundation launched in 1991 by the RAD-AR initiative. It aims at improving, understanding and changing attitudes towards the management and communication of medical benefits and risks

LATENT PERIOD = the period of delay between exposure to a drug and the appearance of an ADE or other outcome

MCA = the UK's governmental Medicines Control Agency

MEDICAID = an insurance scheme to provide access to medical care to the poor in the USA

MORBIDITY RATE = term used to refer to incidence rates of a disease

MORTALITY RATE = rate expressing the proportion of a population that dies within a specified period of time

NATURAL HISTORY = well-defined stages of a disease through which it logically progresses if outside forces do not intervene

NESTED CASE-CONTROL STUDY = a case-control study which recruits both its cases and its controls from the same population, thereby minimising selection bias

NSAID = Non-Steroidal Anti-Inflammatory Drug

OBSERVATIONAL STUDY = a study in which the investigator does not intervene, but simply observes and evaluates changes in one characteristic, e.g. an ADE, in relationship to changes in other variables, e.g. treatments

ODDS = the probability of occurrence of an event, e.g. a congenital malformation, divided by the probability of its non-occurrence, in a defined (e.g. by exposure) population

ODDS RATIO = the ratio between the odds of an exposure to a drug, or other potential causative factor, of interest among cases presenting an ADE and the odds in controls not showing the ADE. *See also* "relative risk"

OTC DRUG = a medicine for which no medical prescription is required and that, therefore, is readily available to the public. Depending upon the country and the product, it may be available via pharmacies only (= PSO, pharmacy sales only), but in certain countries some of these drugs may be sold via department stores

OUTCOME = any one of all possible results that may stem from exposure to a causal factor, or from preventive or therapeutic interventions

OVERREPORTING = tendency to falsely identify and therefore errantly include cases of interest, leading to a false increase of numerator in a rate

PDD = Prescribed Daily Dose, a unit of measurement of drug utilization that is used for ADE incidence calculations

PEM = Prescription Event Monitoring, a system created to monitor for ADEs in a population. Prescribers are identified and requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specific drug

PERIOD PREVALENCE = total number of persons known to have had a disease or to have shown an ADE at any time during a specified time period

PHARMACO-EPIDEMIOLOGY = the science of measuring the use and the effects (beneficial and adverse) of drugs in large, defined populations

PHARMACOVIGILANCE = the continual monitoring for and the study of effects and other safety-related aspects of drugs that have been approved and marketed to the public

PHASE IV STUDY = a controlled or uncontrolled clinical trial, with a carefully defined selection of patients and ditto monitoring parameters

PMS = Post-Marketing Surveillance. This term seems to have various definitions

- In the present context, it is defined as: a large prospective cohort study, conducted after marketing, that screens for ADEs and studies their incidence
- Certain other definitions are close or even identical to that of “pharmacovigilance”

POINT PREVALENCE = number of persons with a disease or showing an ADE at a specified point in time. *See also* “prevalence”

PPA = Prescription Pricing Authority, the agency that collects a copy of all prescriptions in the UK

PPI = Patient Package Insert, a patient-oriented document that explains in lay language what the patient should know about his/her medicine and that is delivered with it

PPO = Preferred Provider Organisation (in USA), a health care organisation that resembles HMOs in many respects. The main difference is that, in contrast to an HMO, physicians are not employed by a PPO. Rather, they have a contract with the PPO to provide medical service for a set (possibly discounted) fee

PREVALENCE = number of individuals with a given characteristic (e.g. ADE) in a given population at risk at a specified point in time

PREVALENCE RATE = the prevalence divided by the number of people at risk

PROCEDURE SELECTION BIAS, *see* “susceptibility bias”

PROXY VARIABLE = variable that measures by indirect means another variable that is of interest but cannot be measured directly

PSA = Prescription Sequence Analysis, a technique for assessing certain ADEs of prescription drugs in large populations. It uses pharmacy-based prescription drug histories and looks for certain “marker drugs” prescribed during and outside the use of the drug to be investigated. The ‘marker drugs’ suggest the presence of a specific medical problem

**RAD-AR** = Risk Assessment of Drugs — Analysis and Response, a project initially started by Ciba-Geigy and later developed into an international initiative supported by various transnational pharmaceutical companies. It is an endeavour to improve the information on drug benefits and risks, and to ensure that this information is communicated effectively to key audiences. It developed into the International Medical Benefit/Risk Foundation which was officially launched in Geneva in 1991

**RATE** = ratio whose numerator is the number of individuals with a given characteristic among the total number of individuals studied during a specified observation period. The latter total number is the denominator

**RATIO** = relationship between any two magnitudes expressed as a quotient or the product of a division

**RBB** = Risk–Benefit Balance

**RECALL BIAS** = systematic error due to differences in accuracy or completeness of recall to memory of prior events among patients with different exposures

**RECHALLENGE** = readministration of a drug to a patient thought to have suffered an ADE upon a previous exposure. Rechallenge is only meaningful if dechallenge has been positive

**RECORD LINKAGE** = method of assembling information contained in two or more records

**REFERENCE RISK** = risk in a population that is comparable to a defined (by exposure) population, except for exposure to the medicine of interest

**REGRESSION TO MEAN** = the phenomenon whereby individuals selected to participate in a study in a manner that relates to the severity of their disease spontaneously tend to improve

**RELATIVE RISK** = the ratio of the risk of a particular ADE in the population exposed to the drug, to the risk in an unexposed (reference) population

**RELIABILITY** = degree to which the results obtained by a measurement technique can be replicated

**RISK** = the probability that an undesirable event (e.g. an ADE), that was absent before, will occur within a stated period of time. Note that two patients may face the same hazard (e.g. hepatotoxicity), but that their risk may differ (e.g. because of the presence of a risk factor in (only) one of them)

**RISK FACTOR** = attribute or drug exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a drug event

**SELECTION BIAS** = error due to systematic differences in characteristics between those who are selected for study and those who are not

**SENSITIVITY** = proportion of truly diseased persons in the screened population who are identified as diseased by the screening test. The probability that any given case will be identified by the test

SIDE-EFFECT = unintended effect associated with the use of a normal dose of a drug in man; the effect may be predictable from the drug's pharmacological properties

SIGNAL = a drug–ADE pair that points to a possible causal relationship that should be explored. The relationship should be unknown or have been only incompletely documented previously

SPECIFICITY = proportion of truly nondiseased persons who are so identified by the screening test. The probability of correctly identifying a nondiseased person with a screening test

SPONTANEOUS REPORTING SYSTEM = system maintained by health authorities or drug companies in which ADE reports are voluntarily submitted from health professionals

STATISTICAL INTERFERENCE = the process of generalizing from a sample of study to the entire population from which those subjects are theoretically drawn

SUSCEPTIBILITY BIAS = bias incurred from an initial lack of comparability in the prognostic expectations of treated and nontreated patients

THERAPEUTIC INDEX = ratio of the toxic to the effective dose of a drug

TROHOC = term coined by A. Feinstein to describe a population, retrospectively defined by an outcome, as often used in case-control studies. (Note that the spelling of “Trohoc” is identical to that of “Cohort”, but in reversed order)

UNDERREPORTING = failure to have all identified cases of interest reported, leading to reduction of numerator in a rate

UNEXPECTED ADE = an ADE whose nature or severity is not described as a possible complication in the current summary of the product's characteristics (e.g. the company's Core Data Sheet, or Investigator's Brochure)

VALIDITY, EXTERNAL = degree to which a specific study result can be extrapolated or applied to subjects other than those included in the study

VALIDITY, INTERNAL = degree to which an assessment measures what it purports to measure; absence of bias or systematic errors. *See also* “reliability”

VALIDITY, MEASUREMENT = expression of the degree to which a measurement instrument measures what it purports to measure

VAMP RESEARCH DATABANK = a “catch all” database with information from computerised GP practices in the UK. Collection of information for this database was unfortunately stopped in November 1993. The existing information has been made available to the UK Department of Health

VITAL STATISTICS = systematically tabulated information concerning births, marriages, divorces, separations, migrations, and deaths based on registrations of these vital events

WHO = World Health Organization