Glossary of Terms

Absolute risk

Risk in a population of exposed persons; the probability of an event affecting members of a particular population (e.g. 1 in 1,000). Absolute risk can be measured over time (incidence) or at a given time (prevalence).

Adverse event

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Adverse drug reaction (ADR)

A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

Allopathy

Non-traditional, western scientific therapy, usually using synthesised ingredients, but may also contain a purified active ingredient extracted from a plant or other natural source; usually in opposition to the disease.

Association

Events associated in time but not necessarily linked as cause and effect.

Attributable risk

Difference between the risk in an exposed population (absolute risk) and the risk in an unexposed population (reference risk), also referred to as excess risk. Attributable risk is the result of an absolute comparison between outcome frequency measurements, such as incidence.Examples: If the exposed persons with a particular outcome are A, the exposed persons without the outcome are B, the unexposed persons with the outcome are C and the unexposed persons with the outcome are D, then the attributable risk is calculated as :

(A+B)] - [C / (C+D)]. If, during the same time period, the incidence of rash in a population treated with medicine X is 35/1,500=0.023, and the incidence of rash in a population not treated with X is 5/2,000=0.0025, the attributable risk is (35/1,500) - (5/2,000) = 0.0205.

Benefit

An estimated gain for an individual or a population. See also Effectiveness/Risk. Benefit - risk analysis Examination of the favourable (beneficial) and unfavourable results of undertaking a specific course of action. (While this phrase is still commonly used, the more logical pairings of benefit-harm and effectiveness-risk are slowly replacing it).

Benefit - risk analysis

Examination of the favourable (beneficial) and unfavourable results of undertaking a specific course of action. (While this phrase is still commonly used, the more logical pairings of benefit-harm and effectiveness-risk are slowly replacing it).

Biological products

Medical products prepared from biological material of human, animal or microbiologic origin (such as blood products, vaccines, insulin).

Causal relationship

A relationship between one phenomenon or event (A) and another (B) in which A precedes and causes B. In pharmacovigilance; a medicine causing an adverse reaction.

Causality assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according established algorithms.

Cem-Flow

Software developed by UMC for collection and analysis of data in Cohort Event Monitoring.

CIOMS

The Council for International Organizations of Medical Sciences (CIOMS) is a body set up under World Health Organization and UNESCO. It has developed a series of guidelines on Pharmacovigilance, drawn up by a committee of volunteers from Industry, regulatory authorities, WHO and others.

The main guidelines concern the international reporting form (CIOMS I); periodic safety update reports (CIOMS II); core data sheets (CIOMS III); benefit-risk assessments (CIOMS

IV); practical issues in Pharmacovigilance (CIOMS V); clinical trial safety data (CIOMS VI); and development safety update reports (CIOMS VII).

Clinical trial

A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety.

Cohort Event Monitoring

Cohort Event Monitoring (CEM) is a prospective, observational study of events that occur during the use of medicines, for intensified follow-up of selected medicinal products phase. Patients are monitored from the time they begin treatment, and for a defined period of time. See also Prescription Event Monitoring.

Common Epidemiology

In Pharmacovigilance, an event with a frequency between 1 in 100 and 1 in 10.

Co-morbidities

Two or more coexisting medical conditions or disease processes that are additional to an initial diagnosis.

Compliance

Faithful adherence by the patient to the prescriber's instructions.

Congenital Anomalies

Morphological, functional and/or biochemical developmental disturbance in the embryo or foetus whether detected at birth or not. The term congenital anomaly is broad and includes congenital abnormalities, foetopathies, genetic diseases with early onset, developmental delay, etc.

Control group

The comparison group in drug-trials not being given the studied drug.

Critical terms

Some of the terms in WHO-ART are marked as 'Critical Terms'. These terms either refer to or might be indicative of serious disease states, and warrant special attention, because of their

possible association with the risk of serious illness which may lead to more decisive action than reports on other terms.

Data mining

A general term for computerised extraction of potentially interesting patterns from large data sets often based on statistical algorithms. A related term with essentially the same meaning is 'pattern discovery'. In Pharmacovigilance, the commonest application of data mining is so called disproportionality analysis, for example using the Information component (IC).

De-challenge

The withdrawal of a drug from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Disproportionality analysis

Screening of ICSR databases for reporting rates which are higher than expected. For drug-ADR pairs, common measures of disproportionality are the Proportional Reporting Ratio (PRR), the Reporting Odds Ratio (ROR), The Information Component (IC), and the Empirical Bayes Geometrical Mean (EBGM). There are also disproportionality measures for drug-drug-ADR triplets, such as Omega (Ω).

Drug Abuse

It is a patterned use of a drug in which the user consumes the substance in amounts or with methods neither approved nor supervised by medical professionals.

Effectiveness/risk

The balance between the rates of effectiveness of a medicine versus the risk of harm is a quantitative assessment of the merit of a medicine used in routine clinical practice. Comparative information between therapies is most useful. This is more useful than the efficacy and hazard predictions from pre-marketing information that is limited and based on selected subjects.

Efficacy

The ability of a drug to produce the intended effect as determined by scientific methods, for example in pre-clinical research conditions (opposite of hazard).

Epidemiology

The science concerned with the study of the factors determining and influencing the

frequency and distribution of disease, injury and other health-related events and their causes in a defined human population for the purpose of establishing programs to prevent and control their development and spread.

Essential medicines

Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness.

EVMPD

The EndraVigilance Medicinal Product Dictionary (EVMPD) has been developed by the European Medicines Agency in collaboration with the EndraVigilance Joint Implementation Group. The main objective of the EVMPD is to assist the Pharmacovigilance activities in the European Economic Area.

EUDRAGENE

Eudragene is a European collaboration that established a collection of DNA samples as a resource for studying genes which influence serious or adverse drug reactions (ADRs). Identifying genes that influence susceptibility to adverse reactions will advance understanding of the basis of adverse drug reactions and may also lead to the development of tests that can predict individual susceptibility to adverse reactions.

Excipients

All materials included to make a pharmaceutical formulation (e.g. a tablet) except the active drug substance(s).

Formulary

A listing of medicinal drugs with their uses, methods of administration, available dose, dosage forms, side effects, etc, sometimes including their formulas and methods of preparation.

Frequency of ADRs

In giving an estimate of the frequency of ADRs the following standard categories are recommended:

Very common* > 10%

Common (frequent) >1% and <10%

Uncommon (infrequent) >0.1% and < 1%

Rare	>0.01% and <0.1%
Very rare*	<0.01%

* *Optional categories*

Generic (multisource product)

The term 'generic product' has somewhat different meanings in different jurisdictions. Generic products may be marketed either under the non-proprietary approved name or under a new brand (proprietary) name. They are usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after the expiry of patent or other exclusivity rights.

Harm

The nature and extent of actual damage that could be caused by a drug. Not to be confused with risk.

Herbal medicine

Includes herbs, herbal materials, herbal preparations and finished herbal products.

Homeopathy

Homeopathy is a therapeutic system which works on the principle that 'like treats like'. An illness is treated with a medicine which could produce similar symptoms in a healthy person. The active ingredients are given in highly diluted form to avoid toxicity. Homeopathic remedies are virtually 100% safe.

Information component (IC)

The Information component (IC) measures the disproportionality in the reporting of a drug-ADR pair in an ICSR database, relative to the reporting expected based on the overall reporting of the drug and the ADR. Positive IC values indicate higher reporting than expected. The IC has also been implemented on electronic health records, to detect interesting temporal relationships between drug prescriptions and medical events.

ICD

International Classification of Diseases (ICD) is the standard diagnostic tool for epidemiology, health management and clinical purposes.

ICH

The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals

Incidence

Number of new cases of an outcome which develop over a defined time period in a defined population at risk.

Individual Case Safety Report (ICSR)

A report that contains 'information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient'.

MedDRA

MedDRA is the Medical Dictionary for Regulatory Activities. WHO-ART, the WHO Adverse Reactions Terminology, is now mapped to MedDRA.

Medical error

"An unintended act (either of omission or commission) or one that does not achieve its intended outcomes."

Member countries

Countries which comply with the criteria for, and have joined the WHO Programme for International Drug Monitoring.

National Pharmacovigilance centres

Organisations recognised by governments to represent their country in the WHO Programme (usually the drug regulatory agency). A single, governmentally recognized centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyse and give advice on all information related to drug safety.

Odds

Probability of an occurrence p divided by the probability of its non-ocurrence $(1 - p)$.

Odds ratio

Ratio of the Odds in a given population and the Odds in another population.

Omega (Ω)

A measure of disproportionate reporting for drug-drug-ADR triplets in ICSR databases, designed to highlight potential signals of drug- drug interactions. Just like the more established disproportionality measures for drug-ADR pairs, Ω is based on a contrast

between the observed and expected number of reports. A positive Ω indicates higher reporting than expected.

Off-label-use

When the medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information

Overdose

Administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorised product information

OTC (Over the Counter) medicine

Medicinal product available to the public without prescription.

Pani-Flow

Software developed by UMC for collection and analysis of data in relation to vaccinations in a pandemic situation.

Periodic Safety Update Report (PSUR)

A systematic review of the global safety data which became available to the manufacturer of a marketed drug during a specific time period. Produced in an internationally agreed format.

Pharmacoepidemiology

Study of the use and effects of drugs in large populations.

Pharmacology

Study of the uses, effects and modes of action of drugs.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem.

Phocomelia

Characteristic deformity caused by exposure to thalidomide in the womb, also very rarely occurring spontaneously. Meaning: limbs like a seal.

Phytotherapy

Western-style, scientific treatment using plant extracts or materials.

Placebo

An inactive substance (often called a sugar pill) given to a group being studied to compare results with the effects of the active drug.

Polypharmacy

The concomitant use of more than one drug, sometimes prescribed by different practitioners.

Post-authorization safety study (PASS)

A pharmacoepidemiological study or a clinical trial carried out in accordance with the terms of the Marketing Authorisation, with the aim of identifying or quantifying a safety hazard relating to an authorized medicinal product.

Post-marketing

The stage when a drug is generally available on the market.

Predisposing factors

Any aspect of the patient's history (other than the drug) which might explain reported adverse events (genetic factors, diet, alcohol consumption, disease history, polypharmacy or use of herbal medicines, for example).

Pre-marketing

The stage before a drug is available for prescription or sale to the public.

Prescription Event Monitoring (PEM)

System created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specified drug. Also more accurately named *Cohort Event Monitoring*.

Prescription Only Medicine (POM)

Medicinal product available to the public only on prescription.

Prevalence

Number of existing cases of an outcome in a defined population at a given point in time.

Prophylaxis

Prevention or protection.

PSUR

The Periodic Safety Update Report (PSUR) is a stand-alone document that allows a periodic but comprehensive assessment of the worldwide safety data of a marketed drug or biological product.

QPPV

Qualified Person responsible for Pharmacovigilance

Rational drug use

An ideal of therapeutic practice in which drugs are prescribed and used in exact accordance with the best understanding of their appropriateness for the indication and the particular patient, and of their benefit, harm effectiveness and risk.

Re-challenge

The point at which a drug is again given to a patient after its previous withdrawal - also see de-challenge.

Record linkage

Method of assembling information contained in two or more records, e.g. In different sets of medical charts, and in vital records such as birth and death certificates. This makes it possible to relate significant health events that are remote from one another in time and place.

Reference risk

Risk in a population of unexposed persons; also called baseline risk. Reference risk can be measured over time (*incidence*) or at a given time (*prevalence*). The unexposed population refers to a reference population, as closely comparable to the exposed population as possible, apart from the exposure.

Regulatory authority

The legal authority in any country with the responsibility of regulating all matters relating to drugs.

Relative risk

Ratio of the risk in an exposed population (absolute risk) and the risk in an unexposed population (reference risk). Relative risk is the result of a relative comparison between

outcome frequency measurements, e.g. incidences.

Risk

The probability of harm being caused; the probability (chance, odds) of an occurrence.

SAEC

The International Serious Adverse Events Consortium (SAEC) is a non-profit consortium formed in October 2007 between industry, academia, the Welcome Trust, and the US Food and Drug Administration to identify genetic variants associated with serious adverse events.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- results in death
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- is life-threatening

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", the following note of clarification is provided:

The term "severe" is not synonymous with serious. In the English language, "severe" is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side effect

Any unintended effect of a pharmaceutical product occurring at normal dosage which is related to the pharmacological properties of the drug.

Signal

Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. The publication of a signal usually implies the need for some kind of review or action.

Summary of Product Characteristics (SPC)

A regulatory document attached to the marketing authorization which forms the basis of the product information made available to prescribers and patients.

Spontaneous reporting

System whereby case reports of adverse drug events are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

SUSAR

An unexpected adverse reaction (UAR) is an adverse reaction that is not consistent with the product information in the SPC.

A suspected unexpected serious adverse reaction (SUSAR) is any UAR that at any dose:

- **a.** Results in death;
- **b.** Is life threatening (i.e. the subject was at risk of death at the time of the event)
- **c.** Refer to an event which hypothetically might have caused death if it were more severe
- **d.** Requires hospitalisation or prolongation of existing hospitalisation;
- **e.** Results in persistent or significant disability or incapacity;
- **f.** Is a congenital anomaly or birth defect.

SUSAR is a serious adverse drug reaction (SAR) that is unexpected or for which the development is uncommon (unexpected issue) observed during a clinical trial and for which there is a relationship with the experimental drug, whatever the tested drug or its comparator.

Teratogen

Environmental factors which can cause congenital abnormalities.

Thalidomide

Drug prescribed in the 1950s as a mild sleeping pill and remedy for morning-sickness for pregnant women. Led to serious birth defects and the start of modern Pharmacovigilance. Returning to favour in treatment of serious diseases such as cancer and leprosy.

Traditional medicines

Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.

Unexpected adverse reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization, or expected from characteristics of the drug.

Vigi-Base

The name of the WHO Global ICSR Database.

Vigi-Flow

Vigi-Flow is a complete ICSR management system created and maintained by the UMC. It is web-based and built to adhere to the ICH-E2B standard. It can be used as the national database for countries in the WHO Programme as it incorporates tools for report analysis, and facilitates sending reports to Vigi-Base.

Vigi-med

Share point based conferencing facility, exclusive to member countries of the WHO Programme for International Drug Monitoring for fast communication of topical Pharmacovigilance issues.

Vigi-Mine

A statistical tool within Vigi-Search with vast statistical material calculated for all Drug-ADR pairs (combinations) available in Vigi-Base. The main features include the disproportionality measure (IC value) stratified in different ways and useful filter capabilities.

Vigi-Search

A search service for accessing ICSRs stored in the Vigi-Base database offered by the UMC to national Pharmacovigilance centres and other third-party inquirers.

WHO-ART

Terminology for coding clinical information in relation to drug therapy. WHO-ART is maintained by UMC.

WHO Drug Dictionary (WHO DD)

The WHO Drug Dictionary is an international classification of drugs providing proprietary and non-proprietary names of medicinal products used in different countries, together with all active ingredients.