GLOSSARY OF TERMS

ETHICS
METHODOLOGY
PHARMACOLOGY
REGULATION
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GLOSSARY - ETHICS

Authorized third party / authorized representative *[Ethics]***:** A representative of an individual who is not competent to provide free and informed consent. The authorized third party acts in the interest of that individual. *(see also Competence, Consent)*

Autonomy *[Ethics]***:** Literally, self ruling. Related to, and sometimes used in lieu of the bioethical principle of respect for persons. Implies intentionality and freedom from coercion or undue influence. In the Kantian tradition, autonomy implies freely embracing a moral obligation.2 In public health, individual autonomy may be limited by interventions applied to populations. (see also: Respect for Persons) An autonomous being is one that has the power of self-direction, possessing the ability to act as it decides, independent of the will of others and of other internal or external factors *(see also Belmont principles)*

Baseline assessment *[Ethics, Methodology]***:** Assessment of subjects as they enter a trial and before they receive any treatment.

Belmont principles *[Ethics]***:** The Belmont principles of beneficence, respect for persons and justice are useful for ensuring that relevant moral concerns are taken into account on a particular issue. The principles should be given consideration in any research situation. (The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (1979) National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research)

Belmont Report *[Ethics]***:** A document identifying the basic ethical principles that should underlie the conduct of biomedical and behavioural research involving human subjects including guidelines to ensure that research is conducted in accordance with the principles

Beneficence *[Ethics,]***:** Literally, doing good; in bioethics, a prima facie principle underlying utilitarian approaches. Implies an obligation to promote benefits of things judged to be good, typically balancing produced goods against risks or harms. In public health, beneficence implies acting in the best interest of the population or society as a whole. *(see also Belmont principles)*

Benefit *[Ethics,]***:** A valued or desired outcome; an advantage. Human research application requests information about the direct benefits accruing to the research participants.

Casuistry A *[Ethics,]***:** Method of practical ethical reasoning emphasising particular cases over theories or principles. From paradigm cases and the selection of morally relevant maxims indicating the right judgment or action, the user of casuistry finds generalisable guidance for judgments and actions when confronted with similar cases. Casuistry is not incompatible with the methods of principalism and specified principalism.

Children*[Ethics, Methodology,]***:**Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be (See also: Assent and Permission).*(see also Vulnerable Subjects)*

Citizens' jury *[Ethics,]***:** Involves a representative sample of 12 to 16 community members who are not in any way affiliated with any political or interest groups particular to the issue being debated. The group meets over a number of days, and the meetings are facilitated by a moderator. Jurors attend plenary sessions, 'cross-examine' witnesses and deliberate on issues, and the conclusions reached are compiled into a report which is distributed to stakeholders and policy makers. The advantage of this approach is that jurors arrive at an informed position, rather than simply providing their initial 'gut' feeling on a particular topic.

Cognitively impaired *[Ethics,]***:** Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behaviour disorders,

or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.*(see also Vulnerable Subjects)*

Communitarianism *[Ethics,]***:** Places the community at the centre of a value system. The individual members of the community are acknowledged: however it is the good of the community, its goals, and the threats it faces that are the key considerations.

Compassionate use *[Ethics,]***:** Method of providing experimental therapeutics prior to final approval by competent authority for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained for "compassionate use" of a drug or therapy

Compensation *[Ethics,]***:** Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. (For comparison, see also: Remuneration.)

Competence *[Ethics, Regulation,]***:** The ability of prospective subjects to give informed consent in accord with their own fundamental values. It involves the ability to understand information presented, appreciate the potential consequences of the decision, and provide free and informed consent (See also: Incompetence, Incapacity.)*(see also Vulnerable Subjects)*

Compounds Insensitive to Ethnic Factors *[Ethics,]***:** A compound whose characteristics suggest minimal potential for clinically significant impact by ethnic factors on safety, efficacy, or dose response.

Compounds Sensitive to Ethnic Factors *[Ethics,]***:** A compound whose pharmacokinetic, pharmacodynamic, or other characteristics suggest the potential for clinically significant impact by intrinsic and/or extrinsic ethnic factors on safety, efficacy, or dose response.

Confidentiality *[Ethics,]***:** One of the important components of medical ethics and a fundamental component in the doctor-patient relationship. Refers to maintaining the confidentiality of trial participants including their personal identity and all personal medical information. The trial participants' consent to the use of records for data verification purposes should be obtained prior to the trial and assurance must be given that confidentiality will be maintained. All personal information about an individual is not to be revealed to third parties without the individual's consent. *(see also Respect for persons, Anonymous data, Indirectly identifying data, Confidentiality)*

Consent *[Ethics, Methodology,]***:** See Informed Consent.

Contract*[Ethics, Methodology,]***:**A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

Declaration of Helsinki *[Ethics, Regulation,]***:** A series of guidelines adopted by the 18th World Medical Assembly in Helsinki, Finland in 1964. The Declaration addresses ethical issues for physicians conducting biomedical research involving humans. Recommendations include the procedures required to ensure subject safety in clinical trials, including informed consent and Ethics Committee reviews. It was revised in 1975 and 1989.

Deontological *[Ethics,]***:** A duty-based theoretical approach to ethics, associated with the philosopher Kant. Right actions stem from freely embraced obligations to universal

moral imperatives, such as the obligation to respect persons as ends and not as means. (see also: Respect for persons)

Directly identifying data *[Database, Ethics,]***:** Information that allows for individuals to be identified or located easily without the need for any additional information. Examples of directly identifying data items include names and residential addresses.

Dissent *[Ethics,]***:** Refusal to participate in research by an individual not able to provide free and informed consent.

Distributive justice *[Ethics,]***:** Distributive justice concerns what is just or right with respect to the allocation of goods (or utility) in a society. It is often contrasted with procedural justice. Distributive justice concentrates on just outcomes, while procedural justice concentrates on just processes. The most prominent contemporary theorists of distributive justice are John Rawls and Robert Nozick..

Duty of care *[Ethics,]***:** A duty to do everything reasonably practicable to protect individuals from harm. Individuals such as doctors or researchers are often held to a higher standard of care, as they are in a position where large numbers of individuals may unquestioningly trust their motives and judgements due to their roles in society. *(see also Obligation)*

Emancipated Minor *[Ethics, Regulation,]***:** A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor)

Equipoise *[Ethics, Methodology,]***:** A condition where there is a balance between different social, emotional, or intellectual influences; something that creates a balanced state, usually by counterbalancing some other force or thing.

Equitable *[Ethics,]***:** Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed. *(see also Justice)*

Ethics *[Ethics,]***:** The practice of applying a code of conduct based on moral principles to day-to-day actions to balance what is fair to individuals or organizations and what is right for society.

Ethics Committee *[Ethics,]***:** See Independent Committee

Ethnic factors *[Ethics,]***:** Are factors relating to races or large populations grouped according to common traits and customs. Note that this definition gives ethnicity, by virtue of its cultural as well as genetic implications, a broader meaning than racial. Ethnic factors may be classified as either intrinsic or extrinsic. (Appendix A)

Guardian *[Ethics, Regulation,]***:** An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

Harms and benefits *[Ethics,]***:** The physical, psychological, social, economic or legal impact of research on a research subject and/or on society. Harms and benefits vary according to the research discipline and the methodology used. They may be difficult to predict.

Healthy volunteer *[Ethics, Methodology,]***:** See voluntary

Helsinki Declaration *[Ethics,]***:** See Declaration of Helsinki.

Human Subjects *[Ethics,]***:** Individuals whose physiologic or behavioural characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1)

data through intervention or interaction with the individual; or (2) identifiable private information. HRC prefers the term "participant" to "subject."

Incapacity *[Ethics,]***:** Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (See also: Incompetence.)*(see also Vulnerable Subjects)*

Incompetence *[Ethics,]***:** A legal term meaning inability to manage one's own affairs, and often used as a synonym for incapacity. (See also: Incapacity.)*(see also Vulnerable Subjects)*

Independent Ethics Committee (IEC)*[Ethics,]***:**An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical/ scientific professionals and nonmedical/ non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favourable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guideline.

Informed consent *[Ethics, Methodology,]***:** A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence. Before carrying out any form of research on an individual, they must be informed about the study's aims, methods, anticipated benefits and any potential risks. The individual must also be informed that they are free to decline to participate in the study and are free to leave at any time without any impact on their treatment. The researcher must then obtain the individual's consent, usually in writing. If this is not possible, non-written consent must be formally documented. *(see also Autonomy)*

Intervention *[Ethics, Methodology,]***:** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes

Justice *[Ethics,]***:** An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; Justice involves considering the fair distribution of the benefits and burdens of research within society. The duty of researchers is to conduct studies that advance knowledge in a given area to potentially benefit all members of the population. However, the advancement of knowledge cannot be at the expense of individual research participants or particular sub-groups of the population. Contrasted with retributive justice operating in the criminal justice system. *(see also Belmont principles)*

Legal incompetence *[Ethics,]***:** A legal state, defined by procedures spelled out in provincial law, that an individual is unable to consent for him or herself. *(see also Vulnerable Subjects)*

Legally Authorized Representative *[Ethics, Regulation,]***:** A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subject research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's

participation in the procedure(s) involved in the research.

Libertarianism *[Ethics,]***:** Places the personal freedom of an individual at the centre of analysis. Personal freedom and autonomy are claimed as rights, unless there is sufficient reason to limit them.

Mature Minor *[Ethics, Regulation,]***:** Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (See also: Emancipated Minor.)*(see also Children)*

Minimal Risk *[Ethics, Methodology,]***:** A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination. The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults

Non-maleficence *[Ethics,]***:** Literally, not causing harm. A prima facie principle in bioethics, sometimes subsumed under the principle of beneficence. An obligation traditionally at the heart of medical ethics—the "first do no harm" component of the Hippocratic Oath—non-maleficence can be seen as distinct from the obligation to produce good (see also: Beneficence) *(see also Belmont principles, Beneficence)*

Nüremberg Code *[Ethics,]***:** As a result of the medical experiments conducted by Nazis during World War II, the US Military Tribunal in Nuremberg in 1947 set forth a code of medical ethics for researchers conducting clinical trials. The code is designed to protect the safety and integrity of study participants.

Obligation *[Ethics,]***:** Used interchangeably with duty. That which is required, although tempered by competing duties. Obligations are correlated with rights. In epidemiology and public health, professional role obligations derive from basic ethical principles and are articulated in codes of professional conduct. *(see also Duty of care)*

Opt off *[Database, Ethics,]***:** Individuals are informed that their personal information may be used for research purposes. Other times, individuals are automatically included in a research database (eg – cervical screening). Instructions are provided as to what should be done if the individual does not wish for their data to be used.

Opt on *[Database, Ethics,]***:** Tick box or similar is provided on a consent form asking the individual if they are willing for their personal information to be used for the research purposes. A website or phone number is also provided where the individual can obtain more information.

Paternalism *[Ethics,]***:** The theory of overriding the decisions of an individual with the intention of benefiting that individual.

Prima facie *[Ethics,]***:** A term used to describe bioethical principles as neither rules of thumb nor absolute prescriptions but rather as binding in all cases unless an obligation found in one principle conflicts with another. In such situations, balancing of competing principles is undertaken using the technique of specification.

Principles *[Ethics,]***:** Four prima facie principles remain at the centre of education and debate in bioethics: beneficence, nonmaleficence, respect for persons, and justice. They provide the source of rules for ethical decisions (for example, truth telling, privacy, informed consent, etc). Rules are not deduced from principles (that is, principalism) but rather arise from specification. Users of

casuistry may also refer to principles when selecting maxims

Prisoner *[Ethics,]***:** An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statue; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution. Note that this includes adjudicated youth. *(see also Vulnerable Subjects)*

Privacy *[Ethics,]***:** the right of an individual to be secure from unauthorized disclosure to third parties of information about oneself, such as that which is contained in medical records.

Proportionism *[Ethics,]***:** acknowledges rules and values, but does not regard them as universal. The theory takes into account the human nature of the individual, the situation, and the intentions behind an individual's actions. A broad idea of doing good is aimed for. Proportionism can be viewed as a compromise between the extremes of absolutism and relativism.

Relativism *[Ethics,]***:** This theory claims that an individual's personal belief or approval is what makes an action morally right. The basic belief is that morality is not grounded in reasoning, and thus it is the individual's feelings or beliefs that are the only possible means for morally justifying an action.

Remuneration *[Ethics, Methodology,]***:** Payment for participation in research. Remuneration should be appropriate for the amount of effort involved, and not excessive and thereby coercive. Remunerations are not considered a benefit.

Respect for persons *[Ethics,]***:** An ethical principle discussed in the Belmont Report. Respect for persons concerns individual autonomy and seeks to ensure that an individual's wishes are respected, even if they differ from those of the researcher. Allowing individuals to provide informed consent, cease participating in the study if they so desire, and keeping any personal information confidential are processes that uphold the dignity and individuality of research participants. From the Kantian tradition: persons should be treated as ends in themselves and not as means to an end. Implies two distinct moral requirements: acknowledge autonomy and protect those with diminished autonomy. *(see also Autonomy, Belmont principles, Condentiality, Deontological, Prima facie, Principles,)*

Rights *[Ethics,]***:** Justified claims made by individuals or groups upon others and based on a system of rules authorising us to affirm or demand what is due. Possessing a right validly constrains others from interfering with the exercise of that right. Moral rights are claims justified by moral principles and are correlated with obligations. In public health, a broadly defined set of human rights are often asserted.

Rights-based ethics *[Ethics,]***:** Concerns whether any proposed actions violate any fundamental human rights or legal rights, such as the right to privacy or the right to free speech. The focus is on moral principle rather than on consequences.

Risk factor *[Ethics, Methodology,]***:** Something that may increase the chance of developing a disease. Some examples of risk factors for cancer include age, a family history of certain cancers, use of tobacco products, certain eating habits, obesity, exposure to radiation or other cancer-causing agents, and certain genetic changes.

Risk-benefit assessment *[Ethics, Methodology,]***:** Any research involving human beings should be preceded by a careful assessment of any possible risks in comparison with potential benefits to the participating individuals and the population as a whole.

Specification *[Ethics, Methodology,]***:**A methodological technique for interpreting a more general ethical principle to bring its implications closer to—to better "apply" it to—actions and decisions. Specification may be used to resolve conflicts among, to balance, or to rank principles. In public health, the Precautionary Principle is a specified version of the more general principle of beneficence (see also: Principles and Principalism)

Subject *[Ethics, Methodology,]***:** A volunteer who participates in a clinical trial, either as a recipient of the experimental treatment, or as a control who receives the standard treatment, or as a healthy volunteer who receives no treatment.

Subjects (Human) *[Ethics, Methodology,]***:** See: Human Subjects. The term "participant" is preferable because it more correctly portrays the participatory aspects of social science research. Sometimes "subject" more accurately describes the role.

Tuskegee Syphilis Study *[Ethics,]***:** From 1932 to 1973, physicians sought to trace the natural history of syphilis by observing 400 African-American men with syphilis in Tuskegee, Alabama. The subjects, poor share-croppers, were enticed into the study with offers of free medical examinations and special free treatments. These special treatments were actually diagnostic procedures such as lumbar punctures. The false belief that treatment was being administered prevented subjects from otherwise seeking medical treatment for their disease. Penicillin was withheld from the subjects after it was found in the 1940s to be a safe and effective treatment. *(see also Belmont Report)*

Universalisability *[Ethics,]***:** A maxim is universalisable if it can consistently be willed as a law that everyone ought to obey. The only maxims which are morally good are those which can be universalized. The test of universalisability ensures that everyone has the same moral obligations in morally similar situations.

Utilitarianism *[Ethics,]***:** Concerns the notion that the 'right' thing to do is that which maximises the good. The outcome of an action is what is considered to be ethically important, with the greatest good for the greatest number of people being pursued.

Utility and Utilitarian *[Ethics,]***:** An approach to ethics asserting that one should always strive to produce the greatest possible balance of good over harm. Historically, identified with social reform movements of 18th century England. Classically expressed as the obligation to produce the greatest good for the greatest number; more recent accounts emphasise optimisation of benefits and harms.

Valid Analysis *[Ethics, Methodology,]***:** This term means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis of the question of interest are: allocation of study participants of both sexes/genders (males and females) and from different racial/ethnic groups to the intervention and control groups by an unbiased process such as randomization; unbiased evaluation of the outcome(s) of study participants; and use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects among the gender and racial/ethnic groups

Valid consent *[Ethics, Methodology,]***:** In order for an individual to provide valid consent they must be capable of communicating their wishes effectively. Age, language difficulties and physical and mental disabilities may prevent a person from either giving or withholding consent. Consent must be given voluntarily and without coercion. The individual must have a complete understanding of the implications and potential consequences of giving consent. The consent given must be specific and current, in

that consent given in particular circumstances cannot be generalised to other similar situations that the individual may be involved in. *(see also Consent)*

Values *[Ethics,]***:** Concepts used to explain how and why things matter. Values are involved wherever we distinguish between things good and bad, better or worse. Values are characterised as scientific, professional, cultural, social, personal, family, religious, and organic (for example, health). Scientific values include: objectivity, accuracy, generalisability, validity and others. Values are pervasive in epidemiology and public health.2

Virtues *[Ethics,]***:** Character traits—neither skills nor techniques— that make an individual a good professional practitioner, and help her to do her work well. For epidemiologists, the virtues of excellence, integrity, honesty, self effacement, and prudence are important examples. Virtue is not easily taught but may be learned by example from mentors.

Voluntary *[Ethics,]***:** Free of coercion, duress, or undue inducement or influence. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.

Vulnerable Subjects*[Ethics,]***:**Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent. *(see also Prisoner)*

Well-being (of the trial subjects) *[Ethics,]***:** The physical and mental integrity of the subjects participating in a clinical trial.

Willowbrook Studies *[Ethics,]***:** From 1956 to 1972, physicians in New York State infected approximately 800 profoundly mentally impaired children with the hepatitis virus at the time of admission to Willowbrook State School in order to study the course of disease from the earliest stages of infection. Entry to Willowbrook was initially most rapid if parents consented to the hepatitis research; later it was the only way for parents to get their children in. *(see also Belmont Report)*

GLOSSARY - METHODOLOGY

Adaptive clinical trials *[Methodology,]***:**A process for improving the efficiency of clinical trials based on interim analyses of clinical data, potentially leading to reductions in overall sample size, shorter project duration, improved quality of results, and reduced costs.*(see also Bayesian approaches)*

Adequate and well-controlled Trial*[Methodology,]***:**An adequate and well controlled trial has the following characteristics: 1 a design that permits a valid comparison with a control to provide a quantitative assessment of treatment effect; 2 the use of methods to minimize bias in the allocation of patients to treatment groups and in the measurement and assessment of response to treatment; and 3 an analysis of the study results appropriate to the design to assess the effects of the treatment.

Adherence *[Methodology]***:** The extent to which the patient continues the agreed-upon mode of treatment or intervention as prescribed *(see also Compliance)*

All randomized subjects *[Methodology]***:** The analysis set that includes all subjects who were randomized to treatment, with these subjects assigned to the treatment group to which they were randomized. Practical considerations, such as missing data, may lead to some subjects in this set not being included in the corresponding analysis.

Analysis plan *[Methodology, Statistics]***:** The strategy for analysis predefined in the statistical section of the protocol and/or protocol amendments. The plan may be elaborated in a separate document (internal to the sponsor) to cover technical details and procedures for implementing the statistical analyses. The plan should be reviewed and possibly updated as a result of the blind review of the data.

Arm *[Methodology]***:** Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more. *(see also Treatment group, control subjects)*

attributable risk *[Methodology]***:** measure of the proportion of disease risk that is attributable to an exposure. *(see also Risk)*

Audit *[Methodology, Regulation,]***:**Audit A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analysed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOP's), good clinical practice (GCP), and the applicable regulatory requirement(s).*(see also Review)*

Baseline *[Methodology]***:** Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

Bias *[Methodology, Statistics]***:** The systematic tendency of any factors associated with the design, conduct, analysis, and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value. Bias introduced through deviations in conduct is referred to as ''operational'' bias. The other sources of bias listed above are referred to as ''statistical.'' *(see also Selection bias)*

Blinding/Masking *[Methodology]***:** A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).*(see also Double blind study, Single blind study)*

Bridging Data Package *[Methodology]***:** Selected information from the Complete Clinical Data Package that is relevant to the

population of the new region, including pharmacokinetic data, and any preliminary pharmacodynamic and dose-response data and, if needed, supplemental data obtained from a bridging study in the new region that will allow extrapolation of the foreign safety and efficacy data to the population of the new region.

Bridging Study *[Methodology]***:** A bridging study is defined as a supplemental study performed in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage and dose regimen in the new region that will allow extrapolation of the foreign clinical data to the new region. Such studies could include additional pharmacokinetic information.

Case control study *[Methodology]***:** A study that compares two groups of people: those with the disease or condition under study (cases) and a very similar group of people who do not have the disease or condition (controls). Researchers study the medical and lifestyle histories of the people in each group to learn what factors may be associated with the disease or condition. *(see also Retrospective study)*

Case or Case study *[Methodology,]***:**A detailed description of a concrete situation requiring ethical analysis and a resultant judgment or action. Cases provide specific circumstances involving a patient (in medical ethics), a study participant or group (in research ethics) or a population (in public health ethics). Cases are typically grouped by subject matter and as such represent the input to the methods of practical ethical reasoning (see also: Casuistry)

Case Report Form (CRF) *[Methodology]***:** A printed, optical, or electronic document designed to record all of the protocolrequired information to be reported to the sponsor on each trial subject

Causality *[Methodology]***:** The relating of causes to the effects they produce. Most of epidemiology concerns causality and several types of causes can be distinguished. It must be emphasized, however, that epidemiological evidence by itself is insufficient to establish causality, although it can provide powerful circumstantial evidence.

Clinical endpoint *[Methodology]***:** A characteristic or variable that reflects how a patient feels, functions, or survives. Clinical endpoints are distinct measurements or analyses of disease characteristics reflecting the effect of a therapeutic intervention in a clinical trial or study *(see also Endpoint)*

Clinical investigator *[Methodology]***:** A medical researcher in charge of carrying out a clinical trial's protocol.

Clinical Research Assistant *[Methodology]***:** Person employed by a sponsor, or by a contract research organization (CRO) acting on a sponsor's behalf, who monitors the progress of investigator sites participating in a clinical study. At some (primarily academic) sites, clinical research coordinators are called CRA’s

Clinical Trial/Study *[Methodology]***:** Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Cohort study *[Methodology]***:** A form of longitudinal study used in medicine and social science. It is one type of Study design. In medicine, it is usually undertaken to obtain additional evidence to refute or support the existence of an association between suspected cause and disease. The cohorts are identified prior to the appearance of the disease under investigation. The study groups, so defined, are observed over a period of time to determine the

frequency of disease among them. The main characteristic is that the study proceeds from cause to effect. *(see also Cross sectional study)*

Co-morbidity *[Methodology, Statistics]***:** The presence of coexisting or additional diseases with reference to an initial diagnosis. Co-morbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. *(see also Morbidity)*

Comparator *[Methodology]***:** An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical trial.

Competent Authorities *[Methodology]***:** See Regulatory Authorities

Complete Clinical Data Package *[Methodology]***:** A clinical data package intended for registration containing clinical data that fulfil the regulatory requirements of the new region and containing pharmacokinetic data relevant to the population in the new region. Ethnic Factors in the Acceptability of Foreign Clinical Data 8

Compliance *[Methodology]***:** Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements *(see also Observance, Adherence)*

Content validity *[Methodology]***:** The extent to which a variable (e.g., a rating scale) measures what it is supposed to measure. Double dummy: a technique for retaining the blind when administering supplies in a clinical trial, when the two treatments cannot be made identical. Supplies are prepared for Treatment A (active and indistinguishable placebo) and for Treatment B (active and indistinguishable placebo). Subjects then take two sets of treatment; either A (active) and B (placebo), or A (placebo) and B (active).

Contract Research Organization (CRO) *[Methodology]***:** A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial related duties and functions

Control (Subjects) or Controls *[Methodology]***:** Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of study. Control conditions may be concurrent (occurring more or less simultaneously with the condition under study) or historical (preceding the condition under study). When the present condition of subjects is compared with their own condition on a prior regimen or treatment, the study is considered historically controlled. The control group serves as a measuring stick to gauge the effectiveness of the experimental treatment. *(see also Arm, Treatment group, Control group)*

Controlled trial *[Methodology]***:** Control is a standard against which experimental observations may be evaluated. In clinical trials, one group of participants is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo. *(see also Placebo, Comparator, Descriptive study)*

Coordinating Committee *[Methodology]***:** A committee that a sponsor may organize to coordinate the conduct of a multicenter trial.

Co-principal Investigator (CO-PI) *[Methodology]***:** The other primary scholar or researcher involved in conducting the research; if the project is for a thesis or dissertation, the student is the co-PI.

CRA *[Methodology]***:** Clinical Research Assistant:

CRF *[Methodology]***:** Case Report Form

Cross sectional study *[Methodology]***:** In survey research, a study in which data are obtained only once. Contrast with longitudinal studies in which a panel of

individuals is interviewed repeatedly over a period of time. Note that a cross sectional study can ask questions about previous periods of time, though. *(see also Cohort study)*

Cross-over design *[Methodology]***:** A clinical trial design in which patients receive, in sequence, the treatment (or the control), and then, after a specified time, switch to the control (or treatment). In this design, patients serve as their own controls, and randomization is used to determine the order in which a patient receives the treatment and control.

Data safety monitoring board (DSMB)*[Methodology,]***:**An independent committee, composed of community representatives and clinical research experts, that reviews data while a clinical trial is in progress to ensure that participants are not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

Debriefing *[Methodology]***:** Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioural sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)

Deductive reasoning (or deduction) *[Methodology]***:** Reasoning from the general to the particular (or from cause to effect) See inductive reasoning *(see also Inductive reasoning)*

Descriptive Study *[Methodology]***:** Any study that is not truly experimental (e.g., quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies). *(see also Controlled trial)*

Dichotomous variable *[Methodology, Statistics]***:** Binary variable *(see also Continuous variable)*

Documentation*[Database, Methodology,]***:**All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

Double blind study *[Methodology]***:** A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study. *(see also Blinding, Single blind study)*

Drop out *[Methodology]***:** A subject in a clinical trial who for any reason fails to continue in the trial until the last visit required of him/her by the study protocol. *(see also Loss to follow-up)*

EBM *[Methodology]***:** Evidence-based medicine

Efficacy (of a drug or treatment) *[Methodology, Pharmacology]***:** The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug 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 FDA, Phase II clinical trials gauge efficacy and Phase III trials confirm it.

Eligibility criteria *[Methodology]***:** Summary criteria for participant selection; includes Inclusion and Exclusion criteria. *(see also Inclusion criteria, Exclusion criteria)*

Endpoint *[Methodology]***:** Overall outcome that the protocol is designed to evaluate.

Epidemiology *[Methodology]***:** The study of the various factors influencing the occurrence, distribution, prevention and control of

disease, injury and other health-related events in a defined human population

Equivalence trial *[Methodology]***:** A trial with the primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences.

Aetiology *[Methodology]***:** The cause of a disease; the study of causes of disease.

Event *[Methodology]***:** This is not the same as "serious," which is based on patient/event outcome

Evidence-based medicine (EBM) *[Methodology]***:** Applies the scientific method to medical practice. According to the Centre for Evidence-Based Medicines Using techniques from science, engineering and statistics, such as meta-analysis of scientific literature, risk-benefit analysis, and randomized controlled trials, it aims for the ideal that healthcare professionals should make "conscientious, explicit, and judicious use of current best evidence" in their everyday practice.

Exclusion criteria *[Methodology]***:** See inclusion criteria

Expedited Review *[Methodology]***:** Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

Explanatory trials [*Methodology]***:** Explanatory questions ask whether a carefully selected group of patients can benefit from a treatment and, if so, by what biological mechanism. Explanatory trials define a population of roughly equivalent risk by imposing strict eligibility criteria, and test a precise hypothesis about the treatment's biological mode of action. The treatment's effect is assessed through endpoints based on the biological mode of action, so follow-up is generally short and the endpoints are usually laboratory measurements, not clinical outcomes. The protocol gives rigid rules for patient management and study drug discontinuation, and any deviation from the protocol must be carefully described, because it may affect the interpretation of the trial.

Extrapolation of Foreign Clinical Data *[Methodology]***:** The generalization and application of the safety, efficacy and dose response data generated in a population of a foreign region to the population of the new region.

Factorial design *[Methodology]***:** Most trials only consider a single factor, where an intervention is compared with one or more alternatives, or a placebo. In a trial using a 2x2 factorial design, participants are allocated to one of four possible combinations. For example in a 2x2 factorial, RCT of nicotine replacement and counselling, participants would be allocated to (a) nicotine replacement alone, (b) counselling alone, (c) both, or (d) neither.

Follow-up*[Methodology,]***:**Process of periodic contact with participants enrolled in the randomized trial for the purpose of administering the assigned interventions, modifying the course of interventions, observing the effects of the interventions, or collecting data.

Foreign Clinical Data *[Methodology]***:** Foreign clinical data is defined as clinical data generated outside of the new region (i.e., in the foreign region). ICH Regions European Union, Japan, The United States of America. New Region The region where product registration is sought. Ethnic Factors in the Acceptability of Foreign Clinical Data 9

Full Board Review *[Methodology]***:** Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in non-

scientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.

GCP *[Methodology]***:** Good Clinical Practice

Generalisability, generalisation *[Methodology]***:** The extent to which the findings of a clinical trial can be reliably extrapolated from the subjects who participated in the trial to a broader patient population.

Global assessment variable *[Methodology, Statistics]***:** A single variable, usually a scale of ordered categorical ratings that integrates objective variables and the investigator's overall impression about the state or change in state of a subject.

GLP (Good Laboratory Practice) *[Methodology]***:**

Good Clinical Practice (GCP)*[Methodology, Regulation,]***:**A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Good Laboratory Practice *[Methodology, Regulation]***:** International regulations that must be observed to ensure high quality experimental standards and reliable data

Historical control *[Methodology]***:** A person, or group of persons, for whom data were collected earlier than for the group being studied. Because of changes over time in risks, prognosis, healthcare, etc. there is a large risk of bias (in studies that use historical controls) due to systematic differences between the comparison groups.

ICH*[Methodology, Regulation,]***:**International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use: a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines

Impartial Witness *[Methodology, Regulation]***:** A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

In silico *[Methodology]***:** Literally "in silicon" and means "performed on computer or via computer simulation." The phrase is derived from the Latin phrases in vivo and in vitro that are commonly used in biology and refer to experiments done in living organisms and outside of living organisms respectively.

In vitro ("In glass") *[Methodology]***:** An artificial environment created outside a living organism (eg, a test tube or culture plate) used in experimental research to study a disease or process.

In vivo *[Methodology]***:** Pertaining to a biochemical process or reaction taking place in a living cell or organism. Compare in vitro

Incidence *[Methodology, Statistics]***:** The frequency of new occurrences of disease within a defined time interval. Incidence rate is the number of new cases of a specified disease divided by the number of people in a population over a specified period of time, usually one year. *(see also Prevalence)*

Inclusion/exclusion criteria *[Methodology]***:** The medical or social standards determining

whether a person may or may not be allowed to enter a clinical trial. These criteria are based on such factors as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

Independent Data Monitoring Committee (IDMC), (Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee)*[Methodology,]***:**An independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

Indication *[Methodology]***:** A sign, symptom, or medical condition that leads to the recommendation of a treatment, test, or procedure.

Inductive reasoning or induction *[Methodology]***:** Is the process of reasoning to a conclusion about an entire class by examining some of its members. See deductive reasoning *(see also Deductive reasoning)*

Inspection *[Methodology]***:** The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies). *(see also Audit)*

Institutional Review Board (IRB)*[Methodology, Regulation,]***:**An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and wellbeing of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Intention-to-treat principle*[Methodology,]***:**The principle that asserts that the effect of a treatment policy can be best assessed by evaluating on the basis of the intention to treat a subject (i.e., the planned treatment regimen) rather than the actual treatment given. It has the consequence that subjects allocated to a treatment group should be followed up, assessed, and analysed as members of that group irrespective of their compliance to the planned course of treatment. *(see also Per protocol)*

Inter- and interpreter reliability *[Methodology]***:** The level of consistency of a rater (intra) or a group of raters (inter) in making an assessment of treatment outcome.

Interim analysis *[Methodology]***:** Any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to the formal completion of a trial.

Interim Clinical Trial/Study Report *[Methodology]***:** A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

Investigational new drug *[Methodology, Pharmacology]***:** a new therapeutic product that has been approved for clinical development. The data generated in lab and animal tests suggest its effectiveness in treating a human disease

Investigational Product *[Methodology, Pharmacology]***:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

GLOSSARY - METHODOLOGY

Investigator *[Methodology]***:** A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. See also Subinvestigator. *(see also Sponsor/investigator)*

Investigator/Institution *[Methodology]***:** An expression meaning ‘‘the investigator and/or institution, where required by the applicable regulatory requirements.’’

Investigator's Brochure *[Methodology]***:** A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of investigational product(s) in human subjects

ITT (Intention to treat) *[Methodology]***:** Intention de traiter*.

Life expectancy *[Methodology]***:** The average number of years remaining for a living being (or the average for a class of living beings) of a given age to live. Life expectancy is also called average life span or mean life span, in distinction to maximum life span. Life expectancy should not be confused with median survival time (the time at which 50% of a cohort will have died).

Loss to follow-up *[Methodology]***:** Loss of contact with some participants, so that researchers cannot complete data collection as planned. Loss to follow-up is a common cause of missing data, especially in long-term studies *(see also Drop out)*

Median survival time*[Methodology,]***:**The time from either diagnosis or treatment at which half of the patients with a given disease are found to be, or expected to be, still alive. In a clinical trial, median survival time is one way to measure how effective a treatment is.

Meta-analysis *[Methodology, Statistics]***:** The formal evaluation of the quantitative evidence from two or more trials bearing on the same question. This most commonly involves the statistical combination of summary statistics from the various trials, but the term is sometimes used to refer to the combination of the raw data

Monitoring *[Methodology]***:** The act of overseeing: the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOP's), GCP, and the applicable regulatory requirement(s).

Monitoring Report *[Methodology]***:** A written report from the monitor to the sponsor after each site visit and/or other trial related communication according to the sponsor's SOP's.

Morbidity *[Methodology]***:** Any departure, subjective or objective, from a state of physiological or psychological well-being. In this sense, sickness, illness, and a morbid condition are synonymous

Morbidity rate *[Methodology]***:** Number of individuals who become ill with a particular disease within a susceptible population during a specified time period

Morbidity table *[Methodology, Statistics]***:** Actuarial statistics showing the frequency and duration of a sickness. *(see also Mortality table)*

Mortality rate *[Methodology, Statistics]***:** The annual number of deaths (from a disease or at general) per 1000 people. *(see also Morbidity rate)*

Mortality table *[Methodology, Statistics]***:** A table showing the incidence of death at specified ages. It shows the number of persons in each age group that die, expressed in terms of deaths per thousand, and based on the deaths in a population of a million persons*(see also Morbidity table)*

Multicenter trial *[Methodology]***:** A trial involving two or more study centres, a common study protocol, and a single analysis plan pooling the data across all centres. *(see also Trial site)*

Nocebo *[Methodology, Pharmacology]***:** The nocebo effect is the phenomenon whereby a patient who believes that a treatment will cause harm actually experiences adverse effects. *(see also Placebo)*

Objective criterion *[Methodology]***:** Critère objectif*.

Observational Study *[Methodology]***:** Type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome (for example, no treatment is given).

Open label trial *[Methodology]***:** A clinical trial in which doctors and participants know which drug or vaccine is being administered.

Order effect *[Methodology]***:** In a repeated measures design, the effect that the order of introducing treatment has on the dependent variable.

Outcome *[Methodology]***:** The impact of care provided to a patient. Outcomes can be positive, such as the ability to walk freely as a result of rehabilitation, or negative, such as the occurrence of bedsores as a result of lack of mobility of a patient*(see also Endpoint)*

Peer review *[Methodology]***:** Review of a clinical trial by experts chosen by the study sponsor. These experts review the trials for scientific merit, participant safety, and ethical considerations.

Per protocol set (valid cases, efficacy sample, evaluable subject's sample) *[Methodology]***:**

Periodic Safety Update Report (PSUR) *[Methodology, Regulation]***:** For a medicinal product with a marketing authorisation: All records of adverse reactions shall be submitted to the competent authorities in form of a periodic safety update report, either immediately upon request or periodically as follows: six monthly for the first two years after authorisation, annually for the subsequent two years, and at the time of the first renewal. Thereafter the periodic safety update report shall be submitted at five-yearly intervals together with the application for renewal of the authorisation. The periodic safety update report shall include a scientific evaluation of the benefit and risks afforded by the medicinal products.

Phase I trials*[Methodology, Pharmacology,]***:**Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients. Phase I: clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80).

Phase II trials *[Methodology, Pharmacology]***:** Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks. Phase II: clinical trials study the biomedical or behavioural intervention in a larger group of people (several hundred)

Phase III trials*[Methodology, Pharmacology,]***:**Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labelling. These studies investigate the efficacy of the biomedical or behavioural intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

Phase IV trials *[Methodology, Pharmacology]***:**Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use... These

studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

Placebo *[Methodology, Pharmacology]***:** A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment. No sick participant receives a placebo if there is a known beneficial treatment. *(see also Nocebo, Control group)*

Population Representative of the New Region *[Methodology]***:** A population that includes the major racial groups within the new region.

Preclinical study *[Methodology]***:** Study that uses live animals or cell cultures to determine the effectiveness and toxicity of a treatment. Preclinical studies take place before any testing in humans is done. *(see also Clinical study, In vitro, In vivo, In silico, Animal model)*

Prevalence *[Methodology]***:** number of cases of a disease, infected persons, or persons with some other attribute present during a particular interval of time. It is often expressed as a rate (for example, the prevalence of diabetes per 1,000 persons during a year). See related Incidence *(see also Incidence)*

Prevention trials *[Methodology]***:** Refers to trials to find better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vitamins, vaccines, minerals, or lifestyle changes.

Principal Investigator (PI) *[Methodology]***:**

Probabilistic matching *[Methodology]***:** the linking of records using mathematical algorithms to determine the likelihood that two or more records from various data sets represent the same individual. The decision on whether two records matched is based on the total 'match score'; often clerical review is undertaken to match scores close to the cut-off value set by the researchers.

Proof of concept *[Methodology]***:** Classically, proof of concept can be viewed as studies that demonstrate the clinical relevance of a novel mechanism to treat a disease. The objectives of Proof of Concept: validation of the relevance of novel therapeutic targets and vivo preclinical models to man; define potential biological markets for clinical efficacy or toxicity

Prospective Study *[Methodology]***:** Study designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective study needs not involve manipulation or intervention but may be purely observational or involve only the collection of data. *(see also Retrospective study)*

Protocol *[Methodology]***:** A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Protocol Amendment *[Methodology]***:** A written description of a change(s) to or formal clarification of a protocol.

QALY *[Methodology]***:** A measure of the outcome of actions (either individual or treatment interventions) in terms of their health impact. If an action gives a person an extra year of healthy life expectancy, that counts as one QALY. If an action gives a person an extra year of unhealthy life expectancy (partly disabled or in some

distress), it has a value of less than one. Death is rated at zero.

Quality Assurance (QA) *[Methodology]***:** All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

Quality Control (QC) *[Methodology]***:** The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

Quality of life QOL *[Methodology]***:** The overall enjoyment of life. Many clinical trials measure aspects of a patient's sense of well-being and ability to perform various tasks to assess the effects that cancer and its treatment have on the patient.

Randomisation *[Methodology]***:** A method based on chance by which study participants are assigned to a treatment group. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant.

Randomised trial *[Methodology]***:** A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial. Occasionally placebos are utilized.

Recruitment *[Methodology]***:** process used by investigators to enrol appropriate subjects into a clinical study, i.e. those selected on the basis of the protocol's inclusion and exclusion criteria.

Registry *[Methodology]***:** a record that chronicles information about all new disease cases, to gain an understanding of the demographic patterns and aetiology of the disease.

Regulatory Authorities *[Methodology, Regulation]***:** Bodies having the power to regulate. In the ICH GCP guideline, the expression ‘‘Regulatory Authorities’’ includes the authorities that review submitted clinical data and those that conduct inspections). These bodies are sometimes referred to as competent authorities.

Research *[Methodology]***:** A systematic investigation (i.e., the gathering and analysis of information) designed to develop or contribute to generalisable knowledge.

Retrospective study *[Methodology]***:** Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research. *(see also Case control study)*

Review (of research) *[Methodology]***:** The concurrent oversight of research on a periodic basis. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis. *(see also Audit)*

Risk *[Methodology]***:** The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (See also: Minimal Risk.)

Screening trials *[Methodology]***:** Refers to trials which test the best way to detect certain diseases or health conditions.

selection bias *[Methodology, Statistics]***:** An error in choosing the individuals or groups to take part in a study. Ideally, the subjects in a study should be very similar to one another

and to the larger population from which they are drawn (for example, all individuals with the same disease or condition). If there are important differences, the results of the study may not be valid *(see also Bias)*

Sequential analysis *[Methodology]***:** A statistical technique in which the sample size is not fixed in advance, rather, sampling is stopped as soon as significant results are observed. The criteria for stopping the trials at each sample size are set so that the overall probability (for all sample sizes) of falsely rejecting the null hypothesis at any step is held to a preset level. Cf. hypothesis test

Significant Difference *[Methodology]***:** A "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data. This definition differs from the commonly used "statistically significant difference," which refers to the event that, for a given set of data, the statistical test for a difference between the effects in two groups achieves statistical significance. Statistical significance depends upon the amount of information in the data set. With a very large amount of information, one could find a statistically significant, but clinically small difference that is of very little clinical importance. Conversely, with less information one could find a large difference of potential importance that is not statistically significant.

Single blind study *[Methodology]***:** A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study. *(see also Blinding, Double blind study)*

Site Visit *[Methodology]***:** A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.

SMR *[Methodology, Statistics]***:** Standardised mortality ratio

Source Data *[Database, Methodology]***:** All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Sponsor *[Methodology]***:** An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial.

Sponsor-Investigator*[Methodology,]***:**An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Standard Operating Procedures (SOP's) *[Methodology]***:** Detailed, written instructions to achieve uniformity of the performance of a specific function.

Standard treatment *[Methodology]***:** A treatment currently in wide use and approved, considered to be effective in the treatment of a specific disease or condition. *(see also Control group)*

Standardised mortality ratio*[Methodology, Statistics,]***:**(SMR) Standardised Mortality Ratio; the rate of deaths relative to national average rates after adjustments have been made for the age structure and relative social status (or deprivation) of the study population.*(see also Mortality rate)*

Stratified sampling *[Methodology, Statistics]***:** A method of sampling from a population. When sub-populations vary considerably, it is advantageous to sample each subpopulation (stratum) independently.

Stratification is the process of grouping members of the population into relatively homogeneous subgroups before sampling. The strata should be mutually exclusive: every element in the population must be assigned to only one stratum. The strata should also be collectively exhaustive: no population element can be excluded. Then random or systematic sampling is applied within each stratum. This often improves the representativeness of the sample by reducing sampling error. It can produce a weighted mean that has less variability than the arithmetic mean of a simple random sample of the population.

Study Coordinators*[Methodology,]***:**are typically members of a research team that are responsible for such things as, recruiting, screening, and enrolling study participants, as well as ensuring the adherence to Good Clinical Practice guidelines.

Subinvestigator *[Methodology]***:** Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). See also Investigator. *(see also Investigator)*

Superiority trial *[Methodology]***:** A trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control).

Surrogate endpoint *[Methodology]***:** An outcome measure that is used in place of a primary endpoint (outcome). Examples are decrease in blood pressure as a predictor of decrease in strokes and heart attacks in hypertensive patients, and increase in T-cell (a type of white blood cell) counts as an indicator of improved survival of AIDS patients. Use of a surrogate endpoint assumes that it is a reliable predictor of the primary endpoint(s) of interest *(see also Clinical endpoint, Endpoint)*

Surrogate variable *[Methodology]***:** A variable that provides an indirect measurement of effect in situations where direct measurement of clinical effect is not feasible or practical.

Surveys *[Methodology]***:** Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

Treatment effect *[Methodology]***:** An effect attributed to a treatment in a clinical trial. In most clinical trials, the treatment effect of interest is a comparison (or contrast) of two or more treatments.

Treatment emergent *[Methodology]***:** An event that emerges during treatment, having been absent pre-treatment, or worsens relative to the pre-treatment state.

Treatment group *[Methodology]***:** The group of participants that receives an experimental treatment. See also control group, standard treatment. **(see also arm, control subjects)*

Treatment trials *[Methodology]***:** Refers to trials which test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.

Trial Site *[Methodology]***:** The location(s) where trial-related activities are actually conducted. *(see also Multicentre trial)*

Unexpected Adverse Reaction *[Methodology, Pharmacology]***:** An adverse reaction, the nature, or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unapproved investigational product or summary of product characteristics (SmPC) for an authorised product).

Unexpected Adverse Drug Reaction *[Methodology, Pharmacology]***:** An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator’s Brochure for

an unapproved investigational product or package insert/summary of product characteristics for an approved product). (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

GLOSSARY-PHARMACOLOGY

Absorption *[Pharmacology]*: In pharmacology absorption is the process that results in the transport or diffusion of the drug from the site of administration to the blood. More commonly, absorption is the process where orally administered drugs get into the blood through the intestinal epithelial cells that has toxic effects on a living organism, when that organism is exposed to a lethal dose of a substance once. In other words, basically a short term version of chronic toxicity.

Addiction *[Pharmacology]*: dependence

Adverse Event (AE) *[Pharmacology]*: An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product

Aliquot [*Pharmacology]*: A portion of a specimen used for testing.

Animal model *[Pharmacology]*: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models.

Area under Curve (AUC) *[Pharmacology]*: The area under the plot of plasma concentration of drug (not logarithm of the concentration) against time after drug administration

AUC *[Pharmacology]*: Area Under Curve

Bid *[Pharmacology]*: Twice a day

Bioavailability *[Pharmacology]*: The percent of dose entering the systemic circulation after administration of a given dosage form. More explicitly, the ratio of the amount of drug "absorbed" from a test formulation to the amount "absorbed" after administration of a standard formulation. Frequently, the "standard formulation" used in assessing bioavailability is the aqueous solution of the drug, given intravenously.

Bioequivalence *[Pharmacology]*: Term in pharmacokinetics used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. If two products are said to be bioequivalent, it means that they would be expected to have the same bioavailability, duration of action and efficacy.

Bioethics *[Pharmacology]*: A field of inquiry and academic discipline at the intersection of ethics and the life sciences.7 Emerging with an emphasis upon problems faced in the practice of medicine and biomedical research, bioethics has overlapping areas of scholarship and application: theory and method, clinical practice, regulatory policy, research practice, cultural and social concerns, 8 and recently, public health and epidemiology (see also: Ethics)

Biopharmaceuticals *[Pharmacology]*: Biopharmaceuticals are generally complex macromolecules derived from recombinant DNA technology, cell fusion, or processes involving genetic manipulation. They include recombinant proteins, genetically engineered vaccines; therapeutic monoclonal antibodies; and nucleic acid based therapeutics, including gene therapy vectors.

GLOSSARY-PHARMACOLOGY

Biotransformation *[Pharmacology]***:** Chemical alteration of an agent (drug) that occurs by virtue of the sojourn of the agent in a biological system

Chronic toxicity *[Pharmacology]***:** Property of a substance that has toxic effects on a living organism, when that organism is exposed to the substance continuously or repeatedly.

Clearance *[Pharmacology]***:** This term describes the drug elimination from the body without identifying the mechanism of the process. Clearance is defined as the volume of fluid cleared of drug from the body per unit of time *(see also Pharmacokinetics)*

Clinical pharmacology *[Pharmacology]***:** The study of pharmacology in relation to clinical science. It is a science which deals with the effects of drugs in healthy volunteers and in patients. In the evaluation process the action and adverse affects of drugs can be measured and compared.

Combination therapy *[Pharmacology]***:** An approach to ethics emphasising communal values, the common good, social goals, and traditional practices. Closely aligned with the cooperative virtues and a community's shared understanding of the good life. Often pitted against liberal individualism (that is, rights based approaches) in its militant forms, a moderate communitarian view makes room for individual rights

Dependence *[Pharmacology]***:** addiction: being abnormally tolerant to and dependent on something that is psychologically or physically habit-forming (especially alcohol or narcotic drugs)

Distribution *[Pharmacology]***:** the process by which a drug reversibly leaves the blood stream and enters extracellular fluid and/or the cells of tissue.

Dosage *[Pharmacology]***:** The quantity of a medicine given per administration, or per day.

Dose minimale efficace *[Pharmacology]***:** Dose minimale requise pour entraîner un effet donné

Dose Regimen *[Pharmacology]***:** The route, frequency and duration of administration of the dose of a medicine over a period of time.

Efficacy (of a drug or treatment) *[Methodology, Pharmacology]***:** The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug 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 FDA, Phase II clinical trials gauge efficacy and Phase III trials confirm it.

Ex vivo *[Pharmacology]***:** Ex vivo is an experimental technique where either the experiment is performed in vivo and then analysed in vitro or where part of the subject is removed, the experiment is performed, and the part is returned. See in vivo and in vitro

Excretion *[Pharmacology]***:** The process of eliminating waste products of metabolism and other materials from an organism that are of no use.

Generic drug *[Pharmacology]***:** A medicine with the same active ingredient, but not necessarily the same inactive ingredients, as a brand-name drug. A generic drug may be marketed only after the original drug's patent has expired.

Half life *[Pharmacology]***:** The time required for half the amount of a drug to be eliminated from the body

GLOSSARY-PHARMACOLOGY

Hypersensitivity reactions *[Pharmacology]***:** An allergic disorder in which the body becomes hypersensitive to particular antigens, which provoke characteristic symptoms whenever they are subsequently encountered.

Idiosyncrasy *[Pharmacology]***:** Specific (and usually unexplained) reaction of an individual to eg a chemical exposure to which most other individuals do not react at all. Examples: some people react to their first aspirin with a potentially fatal shock. General allergic reactions do not fall into this category.

IM *[Pharmacology]***:** Intramuscular.

INN *[Pharmacology]***:** International Non proprietary Name (See also trade name)

Investigational new drug *[Methodology, Pharmacology]***:** a new therapeutic product that has been approved for clinical development. The data generated in lab and animal tests suggest its effectiveness in treating a human disease

Investigational Product *[Methodology, Pharmacology]***:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

IV *[Pharmacology]***:** Intravenous

LD 50: *[Pharmacology]***:** The dose of a substance that will kill half (50%) of the treated test animals when given as a single dose. A measure of acute toxicity.

Me too drug *[Pharmacology]***:** A compound that is structurally very similar to already known drugs, with only minor pharmacological differences.

Metabolism *[Pharmacology]***:** The sum of the processes by which a particular substance is handled (as by assimilation and incorporation or by detoxification and excretion) in the living body

Mutagenicity *[Pharmacology]***:** The property of a chemical that causes the genetic characteristics of an organism to change in such a way that future generations are permanently affected.

Nocebo *[Methodology, Pharmacology]***:** The nocebo effect is the phenomenon whereby a patient who believes that a treatment will cause harm actually experiences adverse effects. *(see also Placebo)*

OD *[Pharmacology]***:** Once a day

Oncogenicity *[Pharmacology]***:** The ability to transform cells to a neoplastic (proliferative) state.

Orphan drug *[Pharmacology]***:** A status granted by the EC since 2000 (since 1983 in USA) to unpatentable medications developed for rare diseases. Orphan drug status gives the drug's manufacturer incentives including a ten-year right to exclusively market the compound., assistance to development planning, reduction of registration fees This protection of unpatentable orphan drugs encourages their development by greatly increasing their profitability

PD *[Pharmacology]***:** Pharmacodynamics

Pharmaceutical form *[Pharmacology]***:** The way the drugs are delivered to the patient.

Pharmacodynamics *[Pharmacology]***:** the study of the biochemical and physiological effects of drugs and the

mechanisms of drug action and the relationship between drug concentration and effect. It is often summarily stated that pharmacodynamics is the study of what a drug does to the body, whereas pharmacokinetics is the study of what the body does to a drug

Pharmacokinetic Study *[Pharmacology]***:** A study of how a medicine is handled by the body, usually involving measurement of blood concentrations of drug and its metabolite(s) (sometimes concentrations in urine or tissues) as a function of time. Pharmacokinetic studies are used to characterize absorption, distribution, metabolism and excretion of a drug, either in blood or in other pertinent locations. When combined with pharmacodynamic measures (a PK/PD study) it can characterize the relation of blood concentrations to the extent and timing of pharmacodynamic effects.

Pharmacokinetics *[Pharmacology]***:** A branch of pharmacology dedicated to the study of the time course of substances and their relationship with an organism or system. In practice, this discipline is applied mainly to drug substances, though in principle it concerns itself with all manner of compounds residing within an organism or system, such as nutrients, metabolites, endogenous hormones, toxins, etc. So, in basic terms, while pharmacodynamics explores what a drug does to the body, pharmacokinetics explores what the body does to the drug.

Pharmacology *[Pharmacology]***:** The study of how chemical substances interact with living systems. If substances have medicinal properties, they are considered pharmaceuticals.

Pharmacovigilance *[Pharmacology]***:** The pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effect, of medicines. It is gaining importance for doctors and scientists as the number of stories in the media of drug recalls increases

Phase I trials *[Methodology, Pharmacology]***:** Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients. Phase I: clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80).

Phase II trials *[Methodology, Pharmacology]***:** Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks. Phase II: clinical trials study the biomedical or behavioural intervention in a larger group of people (several hundred)

Phase III trials *[Methodology, Pharmacology]***:** Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labelling. These studies investigate the efficacy of the biomedical or behavioural intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

Phase IV trials *[Methodology, Pharmacology]***:**Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use... These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

PK *[Pharmacology]***:** Pharmacokinetics

Placebo *[Methodology, Pharmacology]***:** A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment. No sick participant receives a placebo if there is a known beneficial treatment. *(see also Nocebo, Control group)*

PO « per os » *[Pharmacology]***:** By mouth, orally

Population Pharmacokinetic Methods *[Pharmacology]***:** Population pharmacokinetic methods are a population-based evaluation of measurements of systemic drug concentrations, usually two or more per patient under steady state conditions, from all, or a defined subset of, patients who participate in clinical trials.

Prodrug *[Pharmacology]***:** A prodrug is a pharmacological substance (drug) which is administered in an inactive (or significantly less active) form. Once administered, the prodrug is metabolised in the body (in vivo) into the active compound.

Route of administration. *[Pharmacology]***:** It can be intravenous, intramuscularly, subcutaneous, oral, topically, etc

Safety and tolerability*[Pharmacology]***:**The safety of a medical product concerns the medical risk to the subject, usually assessed in a clinical trial by laboratory tests (including clinical chemistry and haematology), vital signs, clinical adverse events (diseases, signs and symptoms), and other special safety tests (e.g., electrocardiograms, ophthalmology). The tolerability of the medical product represents the degree to which overt adverse effects can be tolerated by the subject.

SC *[Pharmacology]***:** subcutaneous

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR) *[Pharmacology]***:** Any untoward medical occurrence that at any dose: - Results in death, - Is life-threatening, - Requires inpatient hospitalization or prolongation of existing hospitalization, - Results in persistent or significant disability/incapacity, or - Is a congenital anomaly/birth defect. (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

SUSAR *[Pharmacology]***:** Serious Unexpected Adverse Reaction

Teratogenicity *[Pharmacology]***:** Potential side effect of some drugs producing physical defects in offspring in utero (i.e., birth defects) such as thalidomide

Therapeutic Dose Range *[Pharmacology]***:** The difference between the lowest effective dose and the highest dose that gives further benefit.

tid *[Pharmacology]***:** thrice a day

Tolerance*[Pharmacology]***:**A condition in which higher doses of a drug are required to produce the same effect as

during initial use; often leads to physical dependence.

Toxicology *[Pharmacology]***:** Study of the adverse effects of chemicals on living organisms. It is the study of symptoms, mechanisms, treatments and detection of poisoning, especially the poisoning of people. The chief criterion regarding the toxicity of a chemical is the dose, i.e. the amount of exposure to the substance. Almost all substances are toxic under the right conditions...

Unexpected Adverse Reaction *[Methodology, Pharmacology]***:** An adverse reaction, the nature, or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unapproved investigational product or summary of product characteristics (SmPC) for an authorised product).

Unexpected Adverse Drug Reaction *[Methodology, Pharmacology]***:** An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product). (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

Wash out period *[Pharmacology]***:** Interruption in ongoing treatment

Xenobiotic [*Pharmacology]***:** A biologically (pharmacologically, endocrinologically, and/or toxicologically) active substance that is not produced endogenously and is, therefore, foreign to a living organism. Examples include drugs, dietary components, carcinogens, and chemicals that have been introduced into the environment by artificial means.

GLOSSARY - REGULATION

Audit *[Methodology, Regulation]*:Audit A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analysed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOP's), good clinical practice (GCP), and the applicable regulatory requirement(s).*(see also Review)*

Good Clinical Practice (GCP)*[Methodology, Regulation]*:A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Good Laboratory Practice *[Methodology, Regulation]*: International regulations that must be observed to ensure high quality experimental standards and reliable data

ICH*[Methodology, Regulation]*:International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use: a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines

Impartial Witness *[Methodology, Regulation]*: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Institutional Review Board (IRB) *[Methodology, Regulation]*:An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and wellbeing of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Periodic Safety Update Report (PSUR) *[Methodology, Regulation]*: For a medicinal product with a marketing authorisation: All records of adverse reactions shall be submitted to the competent authorities in form of a periodic safety update report, either immediately upon request or periodically as follows: six monthly for the first two years after authorisation, annually for the subsequent two years, and at the time of the first renewal. Thereafter the periodic safety update report shall be submitted at five-yearly intervals together with the application for renewal of the authorisation. The periodic safety update report shall include a scientific evaluation of the benefit and risks afforded by the medicinal products.

Regulatory Authorities *[Methodology, Regulation]*: Bodies having the power to regulate. In the ICH GCP guideline, the expression ''Regulatory Authorities'' includes the authorities that review submitted clinical data and those that conduct inspections). These bodies are sometimes referred to as competent authorities.

Competence *[Ethics, Regulation]*: The ability of prospective subjects to give informed consent in accord with their own fundamental values. It involves the ability to understand information presented, appreciate the potential consequences of the decision, and provide free and informed consent (See also: Incompetence, Incapacity.)*(see also Vulnerable Subjects)*

GLOSSARY - REGULATION

Declaration of Helsinki *[Ethics, Regulation]***:** A series of guidelines adopted by the 18th World Medical Assembly in Helsinki, Finland in 1964. The Declaration addresses ethical issues for physicians conducting biomedical research involving humans. Recommendations include the procedures required to ensure subject safety in clinical trials, including informed consent and Ethics Committee reviews. It was revised in 1975 and 1989.

Emancipated Minor *[Ethics, Regulation]***:** A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor)

Guardian *[Ethics, Regulation]***:** An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

Legally Authorized Representative *[Ethics, Regulation]***:** A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subject research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Mature Minor *[Ethics, Regulation]***:** Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (See also: Emancipated Minor.)*(see also Children)*

Approved drugs *[Regulation]***:** Regulatory authority must approve a substance as a drug before it can be marketed. The approval process involves several steps including pre-clinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application by the manufacturer of the drug,

CIOMS *[Regulation]***:** Council for International Organizations of Medical Sciences)

European Directive 2001/20/CE *[Regulation]***:**

HRC *[Regulation]***:** See Human Research Committee.

Institution (medical) *[Regulation]***:** Any public or private entity or agency or medical or dental facility where clinical trials are conducted.

Marketing Authorisation (MA) *[Regulation]***:** A medicinal product must have a valid marketing authorisation before it can be launched onto the market and sold to consumers. Marketing authorisation for a medicinal product can be applied for through the mutual recognition procedure, centralized procedure or national procedure

NCA *[Regulation]***:** National Competent Authorities, see Regulatory Authorities

Permission *[Regulation]***:** The agreement of parent(s) or guardian to the participation of their child or ward in research.

GLOSSARY-STATISTICS

Analysis plan *[Methodology, Statistics]***:** The strategy for analysis predefined in the statistical section of the protocol and/or protocol amendments. The plan may be elaborated in a separate document (internal to the sponsor) to cover technical details and procedures for implementing the statistical analyses. The plan should be reviewed and possibly updated as a result of the blind review of the data.

Bias *[Methodology, Statistics]***:** The systematic tendency of any factors associated with the design, conduct, analysis, and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value. Bias introduced through deviations in conduct is referred to as ‘‘operational’’ bias. The other sources of bias listed above are referred to as ‘‘statistical.’’ *(see also Selection bias)*

Co-morbidity *[Methodology, Statistics]***:** The presence of coexisting or additional diseases with reference to an initial diagnosis. Co-morbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. *(See also Morbidity)*

Dichotomous variable *[Methodology, Statistics]***:** Binary variable *(see also continuous variable)*

Global assessment variable *[Methodology, Statistics]***:** A single variable, usually a scale of ordered categorical ratings that integrate objective variables and the investigator’s overall impression about the state or change in state of a subject.

Incidence *[Methodology, Statistics]***:** The frequency of new occurrences of disease within a defined time interval. Incidence rate is the number of new cases of a specified disease divided by the number of people in a population over a specified period of time, usually one year. *(see also Prevalence)*

Meta-analysis *[Methodology, Statistics]***:** The formal evaluation of the quantitative evidence from two or more trials bearing on the same question. This most commonly involves the statistical combination of summary statistics from the various trials, but the term is sometimes used to refer to the combination of the raw data

Morbidity table *[Methodology, Statistics]***:** Actuarial statistics showing the frequency and duration of a sickness. *(see also Mortality table)*

Mortality rate *[Methodology, Statistics]***:** The annual number of deaths (from a disease or at general) per 1000 people. (*see also Morbidity rate)*

Mortality table *[Methodology, Statistics]***:** A table showing the incidence of death at specified ages. It shows the number of persons in each age group that die, expressed in terms of deaths per thousand, and based on the deaths in a population of a million persons*(see also Morbidity table)*

selection bias *[Methodology, Statistics]***:** An error in choosing the individuals or groups to take part in a study. Ideally, the subjects in a study should be very similar to one another and to the larger population from which they are drawn (for example, all individuals with the same disease or condition). If there are important differences, the results of the study may not be valid *(see also Bias)*

SMR *[Methodology, Statistics]***:** Standardised mortality ratio

Standardised mortality ratio*[Methodology, Statistics]***:**(SMR) Standardised Mortality Ratio; the rate of deaths relative to national average rates after adjustments have been made for the age structure and relative social status (or deprivation) of the study population. (*see also Mortality rate)*

Stratified sampling *[Methodology, Statistics]***:** A method of sampling from a population. When sub-populations vary

considerably, it is advantageous to sample each subpopulation (stratum) independently. Stratification is the process of grouping members of the population into relatively homogeneous subgroups before sampling. The strata should be mutually exclusive: every element in the population must be assigned to only one stratum. The strata should also be collectively exhaustive: no population element can be excluded. Then random or systematic sampling is applied within each stratum. This often improves the representativeness of the sample by reducing sampling error. It can produce a weighted mean that has less variability than the arithmetic mean of a simple random sample of the population.

Alpha error *[Statistics]***:** Type I Error *(see also Beta error)*

Alternative hypothesis *[Statistics]***:** In general, the proposition expressing the particular way the null hypothesis is held to be false. Sometimes referred to as the motivated hypothesis, it usually reflects a difference the researcher hopes to demonstrate. In the ANOVA setting, the usual alternative hypothesis is that the true means of the various groups are unequal. *(see also Null hypothesis.)*

Analysis of Variance (ANOVA) *[Statistics]***:** A statistical technique for defining and segregating the cause of variability affecting a set of observations. This technique provides a basis for analysing the effects of various treatments or variables on the subjects or patients being investigated *(see also Variance)*

ANOVA *[Statistics]***:** Analysis of Variance

Bayes' theorem*[Statistics]***:**A theorem describing how the conditional probability of a set of possible causes for a given observed event can be computed from knowledge of the probability of each cause and the conditional probability of the outcome of each cause

Bayesian approaches *[Statistics]***:** Approaches to data analysis that provide a posterior probability distribution for some parameter (e.g., treatment effect), derived from the observed data and a prior probability distribution for the parameter. The posterior distribution is then used as the basis for statistical inference. *(see also Adaptive clinical trials, Bayes' theorem, Frequentist methods, Odds ratio)*

Beta error *[Statistics]***:** Type II Error *(see also Alpha error)*

Binary variable *[Statistics]***:** A special categorical variable for which only two possible categories exist For example, the variable gender would be a binary variable. The variable ice cream flavour would NOT be a binary variable because it has more than two categories for the responses *(see also Continuous variable)*

Biostatistics *[Statistics]* **:**(Sometimes known as biometrics, though a recent development is the use of biometrics to refer to an entirely different field), most generally, is the application of statistics to biology and, most commonly, to medicine. Because research questions in biology and medicine are various, biostatistics has expanded its domain to include any quantitative, not just statistical, models that may be used to answer these questions. Blind review—The checking and assessment of data during the course of the study, but before the breaking of the blind, for the purpose of finalizing the analysis plan.

Chi2 or c2 *[Statistics]***:** A statistic used to compare frequencies of two or more groups. Researchers often use chi-squares to test nominal data. Also see nominal scale...

Confidence interval *[Statistics]***:** Quantifies the uncertainty in measurement. It is usually reported as 95% CI, which is the range of values within which we can be 95% sure that the true value for the whole population lies. For example, for an NNT of 10 with a 95% CI of 5 to 15, we would have 95% confidence that the true NNT value was between 5 and 15*(see also Variance, Standard deviation)*

confounding variable *[Statistics]***:** A factor that distorts the true relationship of the study variables of central interest by virtue of being related to the outcome of interest but extraneous to the study question and unequally distributed among the groups being compared. For example, age might confound a study of the effect of a toxin on longevity if individuals exposed to the toxin were older than those not exposed.

Contingency table *[Statistics]***:** A table (usually 2 rows and 2 columns) that is often used in epidemiology to show the relationship between disease and exposure. The table can be used to divide persons into the categories of diseased and exposed (a), diseased and not exposed (b), not diseased and exposed (c), and not diseased and not exposed (d):*(see also Chi square, Confidence interval)*

Continuous variable *[Statistics]***:** A variable that can be expressed by a large (sometimes infinite) number of score values. For example, height, temperature, and grade point average are continuous variables. Contrast with dichotomous variable. (*see also Binary variable)*

Correlation *[Statistics]***:** The simultaneous change in value of two numerically valued random variables: the positive correlation between cigarette smoking and the incidence of lung cancer; the negative correlation between age and normal vision

Dependent variable *[Statistics]***:** a variable that is not under the experimenter's control -- the data. It is the variable that is observed and measured in response to the independent variable. (*see also Independent variable)*

Distribution *[Statistics]***:** The frequency of occurrence of the values of a variable. For each possible value of the variable, there is an associated frequency with which the variable assumes that value. frequency histogram: a graphic that displays how many measures fall into different classes, giving the frequency at which each category is seen observed. frequency polygon: a graphic presentation of frequency of a phenomenon that typically uses straight lines and points. (*see also Normal distribution, Poisson distribution)*

Frequentist methods*[Statistics]***:**Statistical methods, such as significance tests and confidence intervals, which can be interpreted in terms of the frequency of certain outcomes occurring in hypothetical repeated realizations of the same experimental situation. *(see also Bayesian approaches)*

Geometric mean *[Statistics]***:** The appropriate measure of central tendency on a multiply-divide scale. On the Standard Celeration Chart you derive a geometric mean by multiplying N number of frequencies and then taking the Nth root of that *(see also Mean, Harmonic mean, Median, Mode)*

Harmonic mean *[Statistics]***:** A harmonic mean is used when the influence of extreme values is to be minimized. The harmonic mean of n numbers expressed as the reciprocal of the arithmetic mean of the reciprocals of the numbers *(see also Mean, Geometric mean, Median, Mode)*

Independent variable *[Statistics]***:** a variable that is manipulated, measured, or selected by the researcher as an antecedent condition to an observed behaviour. In a hypothesized cause-and-effect relationship, the independent variable is the cause and the dependent variable is the outcome or effect. (*see also Dependent variable)*

Interaction (qualitative and quantitative) *[Statistics]***:** The situation in which a treatment contrast (e.g., difference between investigational product and control) is dependent on another factor (e.g., centre). A quantitative interaction refers to the case where the magnitude of the contrast differs at the different levels of the factor, whereas for a qualitative interaction the direction of the contrast differs for at least one level of the factor.

Latin square *[Statistics]***:** A Latin square is an n × n table filled with n different symbols in such a way that each symbol occurs exactly once in each row and exactly once in each

column. Here are two examples *(see also Analysis of variance)*

Logistic regression *[Statistics]***:** a statistical technique that predicts the probability of a dichotomous dependent variable (eg, dead or alive) using, typically, a combination of continuous and categorical independent variables *(see also Regression)*

Mean*[Statistics]***:**A type of average (measure of central tendency), which is defined as the sum of all the values in a set of numerical data divided by n; this value is usually the most common usage of the word "average," and typically it is labelled as either μ (lowercase Greek letter "mu") or m to denote a population mean or x (referred to a "x bar") to denote a sample mean*(see also Mean, Geometric mean, Harmonic mean, Median, Mode)*

Median *[Statistics]***:** The midpoint in a series of numbers; half the data values are above the median, and half are below. For example, in the odd series 1, 4, 9, 12 and 33, 9 is the median. In the even series 1, 4, 10, 12, 33 and 88, 11 is the median (halfway between 9 and 12). Note the median is not necessarily the same as the average (or mean). For example, the median of 2, 6, 10, 22 and 40 is 10 but the average is 18*(see also Mean, Geometric mean, Harmonic mean, Median, Mode)*

Mode *[Statistics]***:** The mode is the value that has the largest number of observations, namely the most frequent value or values. The mode is not necessarily unique, unlike the arithmetic mean. (*see also Mean, Geometric mean, Harmonic mean, Median, Mode)*

Multiple logistic regression *[Statistics]***:** Kind of logistic regression in which there are many variables, including several exponential factors

Negative predictive value *[Statistics]***:** The probability that an individual does not have the tested condition, given that the test result is negative. (*see also Positive predictive value)*

Normal distribution *[Statistics]***:** The frequency of a data distribution simulating a bell-shaped curve that is symmetrical around the mean and exhibits an equal chance of a data point being above or below the mean. (syn: Gaussian distribution) *(see also Poisson distribution)*

Null hypothesis *[Statistics]***:** The proposal that no difference exists between groups or that there is no association between risk indicator and outcome variables. If the null hypothesis is true then the findings from the study are the result of chance or random factors. In clinical trials, the prediction that there is no relationship between your treatment and your outcome. see alternative hypothesis *(see also Alternative hypothesis)*

Odds ratio *[Statistics]***:** The odds ratio is a measure of effect size particularly important in Bayesian statistics and logistic regression. It is defined as the ratio of the odds of an event occurring in one group to the odds of it occurring in another group, or to a sample-based estimate of that ratio. The increased use of logistic regression in medical and social science research means that the odds ratio is commonly used as a means of expressing the results in some forms of clinical trials, such as case-controlled trials, and in survey research. It is often abbreviated "OR" in reports. (*see also Bayesian approaches)*

P value *[Statistics]***:** Refers to the probability that the result obtained could have happened by chance. Usually refers to a number derived from a calculation in the study and is displayed as p_ 0.05 or p_ 0.01 or such. This means the likelihood of such a result by chance is less than one in twenty or one in a hundred. The custom is to consider p values of 0.05 or less to signify a significant result, one highly unlikely to happen by chance. (*see also Significance level, Statistical significance)*

Paired data *[Statistics]***:** Data that consists of pairs of related observations eg blood pressure measurement before and after exercise, or data from a matched case-control study. For each observation in one sample

there is a corresponding observation in the other sample. The samples are usually of equal size *(see also Case control)*

Parametric test *[Statistics]***:** A test that measures the value of a parameter on the output or a particular point of an assembly. (*see also Statistical test)*

Percentile *[Statistics]***:** A descriptive measure used to characterize a set of numbers. For example, if the 8th percentile of a set of 200 numbers has the value 27, then 8 percent of the numbers (16 numbers) are less than 27; the median of the set is the 50th percentile*(see also Distribution, Quartile)*

Poisson distribution *[Statistics]***:** A mathematical expression giving the probability of observing various numbers of a particular event in a sample when the mean probability of that event on any one trial is very small. (*see also Distribution, Normal distribution)*

Positive predictive value *[Statistics]***:** The probability that an individual with a positive test has, or will develop, a particular disease, or characteristic, that the test is designed to detect. (*see also Negative predictive value)*

Predictive value *[Statistics]***:** The statistic generated by dividing the number of true positives by the sum of the true positives and false positives (eg the number of cases with truly good care divided by the sum of the cases with truly good care plus those cases classified with good care who did not receive it - i.e., the likelihood that a patient classified as the recipient of good care actually received good care)

Q1, Q2, Q3 *[Statistics]***:** See quartile

Quartile *[Statistics]***:** One of four segments of a distribution that has been divided into quarters. For example, the second-from-the-bottom quartile of an income distribution is those whose income exceeds the incomes of from 25% to 50% of the population. The three quartile points that lie between the extremes of the distribution are designated as Q 1, Q 2, and Q 3 and are defined in terms of the distribution function F(x) as follows: Thus, Q 2 coincides with the median. (*see also Distribution, Percentile, Q1, Q2, Q3)*

SD *[Statistics]***:** Standard deviation

Significance level *[Statistics]***:** A test is the maximum probability that the observed statistic would be observed under the null hypothesis that is considered consistent *(see also P value, Statistical significance)*

Standard deviation *[Statistics]***:** In probability and statistics, the standard deviation is the most common measure of statistical dispersion. Simply put, standard deviation measures how spread out the values in a data set are. More precisely, it is a measure of the average distance of the data values from their mean. If the data points are all close to the mean, then the standard deviation is low (closer to zero). If many data points are very different from the mean, then the standard deviation is high (further from zero). If all the data values are equal, then the standard deviation will be zero.

Standard Error Mean *[Statistics]***:** A measure of variability. The standard error of the mean quantifies how accurately the true population mean is known. A measure of the variability of the mean of the sample as an estimate of the true value of the population mean. The larger the sample size the smaller the standard error of the mean. Used in computing confidence intervals. In a clinical trial, the larger the sample size the tighter the 95% CI is around the point estimate of the study *(see also Standard deviation, Variance)*

Statistical significance *[Statistics]***:** In statistics, a result is significant if it is unlikely to have occurred by chance, given that in reality, the independent variable (the test condition being examined) has no effect, or, formally stated, that a presumed null hypothesis is true. See also Significant Difference. (*see also Significance level, Significance level)*

GLOSSARY-STATISTICS

Statistical test *[Statistics]***:** Type of statistical procedure that is applied to data to determine whether the results are statistically significant (that is, the outcome is not likely to have resulted by chance alone) *(see also t test)*

Statistics *[Statistics]***:** branch of mathematics that deals with the collection and interpretation of numerical information

Survival analysis *[Statistics]***:** A branch of statistics which deals with death in biological organisms and failure in mechanical systems. This topic is called reliability theory or reliability analysis in engineering, and duration analysis or duration modelling in economics. Death or failure is called an "event" in the survival analysis literature, and so models of death or failure are generically termed time-to-event models.

t test *[Statistics]***:** A statistical test which computes the probability (p) that two groups of a single parameter are members of the same population. The population must follow at distribution. However, at test is robust enough to allow considerable deviation from normality

Type I Error (alpha error) *[Statistics]***:** A rejection of a hypothesis when it is true. An example of Type 1 Error is finding a substance efficient when it is not... This is an error of "seeing too much in the data

Type II Error (beta error) *[Statistics]***:** An acceptance of a hypothesis when it is false. An example of Type II Error is not finding a substance present when it is present. This is an error of "not seeing enough in the data."

Type III error *[Statistics]***:** A Type III error consists of correctly rejecting the null hypothesis, but incorrectly attributing the cause. In other words, the researcher correctly identifies an effect, but incorrectly attributes the cause of the effect.

Variance *[Statistics]***:** A measure of the spread of the values in a distribution. The larger the variance, the larger the distance of the individual cases from the group mean. (*see also Standard deviation, Analysis of variance, Confidence interval)*