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INPACT Platform

ACRONYM and GLOSSARY

Our acronym and glossary serves as a reference tool designed to decode the specialized terminology and jargon inherent in the field of medicine making. Whether you're navigating our modules, engaging in pharmaceutical discussions, or delving into the intricacies of drug development, our glossary wants to provide clear and concise explanations to enhance your understanding and facilitate effective understanding and communication within the realm of medicine production.

ACRONYM	DEFINITION
3R	Replacement, Reduction and Refinement
ADA	American Diabetes Association
ADME	Absorption, Distribution, Metabolism, Excretion
AID	Automated Insulin Delivery
CGM	Continuous Glucose Monitor
CMC	Chemistry, Manufacturing, Control
CRA	Clinical Research Associate
CRO	Clinical Research Organization
CT	Clinical Trial
CTA	Clinical Trial Application
CTS	Clinical Trial Site
DMTs	Disease Modifying Therapies
DNA	Deoxyribonucleic Acid
EC	Ethics Commitee
EMA	European Medicines Agency
FDA	Food and Drug Administration
FIH	First in Human
FPG	Fasting Plasma Glucose
GADA	Glutamic Acid Decarboxylase Autoantibodies
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
HbA1c	Glycated Hemoglobin
HTA	Health Technology Assessment
IA	Islet autoantibody
IA-2A	Insulinoma Associated-2 Autoantibodies
IAA	Insulin Autoantibodies
INPACT	INNODIA People with Type 1 Diabetes Community
MAA	Marketing Authorization Application
MAD	Multiple Ascending Dose
MoA	Mode of Action
MTD	Maximum Tolerated Dose
NCA	National Competent Authority
NIS	Non-Interventional Studies
OGTT	Oral Glucose Tolerance Test
OoC	Organs-on-a-chip
PwD	Person with Diabetes
RA	Regulatory Authorities
RC	Recommended Dose
RCT	Randomized Controlled Trial
RPG	Random Glucose Test
SAD	Single Ascending Dose
T1D	Type 1 Diabetes
ZnT8A	Zinc transporter 8 autoantibody

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The glossary content has been provided by EUPATI (European Patients' Academy on Therapeutic Innovation) and has been complemented by INNODIA specifically in connection with Type 1 Diabetes.

• **Clicking on a specific letter** will direct you to the terms within the glossary that begin with that letter, streamlining your search and allowing for easy access to the relevant definition.
• Alternatively, enable **Bookmarks in the sidebar** of your pdf document to conveniently navigate through the document and locate specific terms

A

ABSORPTION
In pharmacology and pharmacokinetics, absorption is the process whereby medicines are transported or taken up from the site of administration (by mouth, inhalation, intravenous or intramuscular injection, etc.) to the blood through capillary, osmotic, solvent, or chemical action in the cells. This could be through the intestinal wall, skin, or mucous membranes.

In specific situations, such as intravenous (IV) therapy, absorption is straightforward and there is less variability, because the medicine goes directly in to the bloodstream. In the case of IV injection, the bioavailability of the compound is 100%.

Absorption is a primary focus in medicines development, as a compound must first be absorbed before any medicinal effects can take place. Moreover, the medicine's pharmacokinetic profile can be significantly changed by factors that affect absorption.

ACTIVE MOLECULE
In medicines, an active molecule is a chemical compound that has pharmacological or biological activity likely to be therapeutically useful.

ADAPTIVE DESIGN
The option to modify the design of an ongoing clinical trial is becoming increasingly common and is known as adaptive design. Data are evaluated before the trial is finished. This is known as interim analysis and might be carried out at several time points. Depending on the circumstances, this may lead to changes to the trial such as stopping one treatment arm or changing the number of participants in a group. The planned number of participants might be reduced if the interim analysis shows that a smaller sample size will still allow a valid result to be obtained. Alternatively, the sample size might be increased if that will allow a valid or reliable result to be obtained within a more acceptable period of time.

Adaptive designs can save time and resources, and can reduce the exposure of study participants to the inferior treatment.
Interim analyses and any anticipated changes to a trial should be described and justified in the study protocol.

ADVERSE DRUG REACTION
A response to a medicinal product which is harmful and unintended. Response in this context means that a causal relationship between the medicinal product and an adverse event is at least a reasonable possibility.

ADVERSE EVENT
Any untoward (not favorable) medical occurrence in a patient, or clinical trial participant receiving a medicine, and which does not necessarily have a causal relationship with this treatment.

Adverse events can therefore be: any unfavorable and unintended sign (e.g.; an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicine, whether or not considered related to the medicine.

ADVERSE DRUG REACTION
An adverse reaction is any adverse event or experience related to a medicine for which a reasonable causal relationship with the medicine's use is suspected. This is synonymous with adverse drug reaction (ADR).

ALLOGENEIC CELLS
Allogeneic cells are cells obtained from a donor, such as bone marrow or umbilical cord blood.

AMES TEST
The Ames test is a biological assay that uses bacteria to analyze whether a chemical can cause mutations in the DNA. A positive test indicates that the chemical is mutagenic and therefore may act as a carcinogen.

ANONYMISE
The removal of personal information (such as names or addresses of clinical trial participants) so that people using trial data cannot identify the individuals who took part. Truly anonymized data contain no information that could reasonably be used, by anyone, to identify individuals - even by cross-checking the data against other sources of information. Anonymous data are data that have had personal information removed.

ANONYMOUS
Anonymous data has had all personal information (such as names or addresses of clinical trial participants) removed, so that people using trial data cannot identify the individuals who took part. Truly anonymized data contain no information that could reasonably be used, by anyone, to identify individuals "even by cross-checking the data against other sources of information. Anonymous data are data that have had personal information removed.

ANONYMOUS CODING SYSTEMS (ACS)
Sets of data from individuals in a trial are given unique codes so they can be stored and managed properly. Anonymous coding systems (ACS) use codes that do not relate to personal information that might be used to identify the individual in any way (for example, a participant's initials or health record number must not be included in the code). This allows individuals taking part in clinical trials to remain anonymous.
Coding can be important to allow tracing of individuals in the future (for example to allow authorized health professionals to follow up on results that come out of trials). To enable this, information about which individual was given which code is usually held securely, for example at a separate location not involved in the trial.

ANTIBODY (Ab)
An antibody (Ab), also known as an immunoglobin, is a protein produced by the body's immune system when it detects harmful substances (called antigens). Antibodies recognize and latch onto antigens in order to neutralize them. An antibody can be also be manufactured in a laboratory to target a specific antigen found on cells associated in various diseases, triggering an immune response that lead to the destruction of the cells carrying the specific antigens. This type of therapy is called target therapy. For instance, Teplizumab is an antibody used in the treatment of Type 1 Diabetes (T1D) which recognize the CD30 antigen present of the surface of T cell, thereby inhibiting the initiation of autoimmune response against the ß cells.

ANTIGEN (Ag)
Any substance capable of stimulating an Immune response. Antigens are typically proteins found on the surface of pathogens such as bacteria, viruses but they can also be chemicals (Insect or snake venom). They can originate from outside the body (exogenous antigens), or from within the body (endogenous antigens). Self-antigens are molecules naturally produced by the body, and play a crucial role in helping the immune system to recognize between the body's own cells and invaders. Self-antigens are essential for maintaining immune tolerance, which prevents the immune system from attacking the body's own tissues and causing autoimmune diseases. Auto-antigens, are a subset of self-antigens that trigger an immune response in autoimmune diseases. In autoimmune diseases, the immune system mistakenly recognizes self-antigens as foreign invaders and mounts an immune response against them, leading to tissue damage and inflammation.

AREA UNDER THE CURVE (AUC)
In the field of pharmacokinetics, the Area Under the Curve (AUC) is the region under a plotted line in a graph of medicine concentration in blood plasma over time. Typically, the area is calculated starting from the time the medicine is administered until the time when the concentration in plasma is insignificant. AUC represents the total exposure that the body receives to an active substance, and helps to evaluate and compare bioavailability profiles between medicines. The time at which the highest concentration of the active substance is found in the blood is called Tmax, and the maximum concentration of the active substance found in the blood stream is called Cmax.

ARM
In clinical research this refers to any of the treatment groups in a randomized trial. Many randomized trials have two arms or groups, but some may have three or even more.

ATTRITION
Attrition is the loss of participants during a clinical trial it is also known as the 'drop-out rate'. The opposite of

attrition is 'retention'.
Attrition can cause bias in study results if more participants drop out of one study arm than another, or if there is a difference between the participants who drop out and those who continue. Attrition can affect how applicable the results of a study are (external validity), or the statistical power of a study.
Research suggests that using a combination of strategies can avoid attrition of participants in trials. Many different methods may be appropriate, for example providing incentives for taking part, giving personal reminders of appointments, and involving patients and/or their carers throughout the trial-design process.

AUDIT
Audits (independent evaluations of activities, processes and product quality) are an element of quality management in industry, finance, commerce and public service. They are typically performed by an independent auditing service, but may also be conducted as an internal audit (self-inspection) by the company through a specific audit department usually directly reporting to the board.
In medicines development, two audit types are routine and required:
1) Good Manufacturing Practice (GMP) audits (self-inspections) to monitor the implementation and compliance with good manufacturing practice principles (required as per Directive 2003/94/EC) and other quality standards like ICH Q10 and to propose necessary corrective measures.
2) Good Clinical Practice (GCP) audits, a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data was recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s) (ICH E6 Directive 75/318/EEC as amended

AUTOANTIBODY
An autoantibody is an antibody (a type of protein) produced by the immune system that is directed against one or more self-antigens.

AUTOIMMUNE REACTION
An autoimmune reaction occurs when the body's immune system mistakenly targets and attacks its own tissues, organs or cells perceiving them as foreign invaders. In autoimmune diseases, the immune system fails to distinguish between self and non-self antigens, leading to inflammation, tissue damage, and dysfunction of the affected organs or systems. Examples of autoimmune diseases include type 1 diabetes.

AUTOLOGOUS
Autologous tissue or cells are tissue or cells derived from the same individual. For example, skin transferred from one part of the body to another is autologous tissue in advanced therapies, stem cells are removed, stored, and later given back to the same person. Autologous transplants are used to treat a number of different blood cancers. Autologous stem cell transplantation is distinguished from allogeneic stem cell transplantation, where the donor and the recipient of the transplanted stem cells are different people.

B

BASAL OR BACKGROUND INSULIN
The basal insulin level refers to the amount of insulin that the body constantly releases to maintain blood glucose levels within a normal range during periods of fasting or between meals. This baseline level of insulin secretion helps to regulate glucose metabolism and prevents blood glucose from rising too high or dropping too low.

BASELINE ASSESSMENTS
Baseline assessments are carried out with participants as they enter a trial and before they receive any treatment.
These assessments may take the form of interviews, questionnaires, physical examinations, laboratory tests, or other procedures. Baseline assessments include demographics (such as age, gender), patient characteristics (such as height, weight, blood pressure), and measurements specific to the study (such as disease characteristics or previous treatment).

BASELINE DATA
Baseline data provide information about participants as they enter a trial and before they receive any treatment.
Baseline data collection may take the form of interviews, questionnaires, physical examinations, laboratory tests, or other procedures. Baseline data include demographics (such as age, gender), patient characteristics (such as height, weight, blood pressure), and measurements specific to the study (such as disease characteristics or previous treatment).

BASIC RESEARCH
Experimental or theoretical research aimed at expanding scientific knowledge and understanding fundamental principles, without specific application pre-defined.

BENEFIT
Benefit is a positive outcome (such as the relief of symptoms, cure, or prevention) from using a treatment or taking part in a study. The benefits of taking part in research may include helping others by participating in medical research, close monitoring by health professionals and experts, or getting access to an effective treatment before it is made available to the wider patient population.

BENEFIT-RISK ASSESSMENT
In medicines, benefit-risk assessment is the continuous examination of the favorable and unfavorable results of a specific treatment to determine whether its benefits outweigh its risks in a -specific condition. It takes into account the evidence on safety and efficacy, as well as other factors like the nature and severity of the condition the medicine is intended to treat or prevent.

BEST SUPPORTIVE CARE (BSC)
Best supportive care is the treatment of choice when a cure is not achievable with existing treatments. It involves the management of disease-related symptoms.

BIAS
In clinical trials, bias is the systematic deviation from true values of treatment effect through the intentional or unintentional adjustment of results. Bias can result from aspects of trial design, the way a trial is carried, or the way the results are analyzed or evaluated.
Bias can be 'operational' - when it arises because of the way a trial is carried out or 'statistical' - when it arises because of trial design or the way results are analyzed or evaluated.
For example, poor trial design might mean that participants at lower risk of experiencing a symptom are placed in one treatment arm as opposed to another treatment arm. Excluding data from certain participants because of knowledge of their outcomes would also cause bias in a trial.
The most important design techniques for avoiding bias in clinical trials are blinding and randomization. The potential effect of bias should also be taken into account during statistical analysis of trial data.

BIG DATA
Big data is the combination and analysis of very large and diverse sets of data, such as non-health and health data, ongoing generation of information about the real-world use of medicines, patient-generated data from social media, and wearable devices.

BIOASSAY
A common short term used for biological assay or assessment. It is a type of scientific experiment that involves the use of live animals, plants, tissues or cells to determine the biological activity of a substance. Bioassays are essential in the development of new medicines.

BIOBANK
A biobank is a large, organized collection of samples, usually human, used for research. Biobanks catalogue and store samples using genetic, clinical, and other characteristics such as age, gender, blood type, and ethnicity. Some samples are also categorized according to environmental factors, such as whether the donor had been exposed to some substance that can affect health. Biobanks play a crucial role in biomedical research, such as in genomics and personalized medicine. Researchers access biobanks when they need samples with similar characteristics for their research studies.

BIOEQUIVALENCE
Bioequivalence means that the identical active pharmaceutical ingredient of two medicines have the same rate and extent of absorption. The medicines produce the same effect at the required target. For example, a receptor in the brain can be a target for a medicine. Bioequivalence is often used to compare an original and generic version of a medicine, or two different formulations (for instance, tablet or oral suspension) of the same medicine.

BIOEQUIVALENCE STUDY
A bioequivalence study is a study conducted to show that two medicines, or two different dosages of the same medicine, are equally absorbed after administration and produce the same effect at the required site.
For generic medicinal products, the concept of bioequivalence is fundamental since the bioequivalence with the reference (original) medicinal product must be demonstrated for a generic to be approved. Regulatory authorities evaluate bioequivalence by considering two standards: the rate of absorption and the extent of absorption. If a medicine formulation differs in one or both parameters, the authorities would determine that this medicine is not bioequivalent to the original product.

BIOETHICS
Bioethics is the application of ethics to the fields of medicine, biomedical research and health policy. It has become an important area of enquiry as advances are made especially in genetic medicine and reproduction. The ethical aspects of research and policy are often included under the title 'ELSI', which stands for 'ethical, legal and social issues'.

BIOLOGIC MEDICINE
A biologic medicine is any medicinal product manufactured in, extracted from, or synthesized in part from biological sources. Biologics can be composed of sugars, proteins, or nucleic acids they may be complex combinations of sugars, proteins, or nucleic acids.

BIOMARKER
A biological marker is something that can be measured which points to the presence of a disease, a physiological change, response to a treatment, or a psychological condition. For example, glucose levels are used as a biomarker in managing diabetes, and brain images can provide information about the progression of multiple sclerosis.
Biomarkers are used in many scientific fields. They are used in different ways at different stages of medicines development, including in some cases as a surrogate endpoint to indicate and measure the effect of interventions, such as medicines, in trials.

BIOSIMILAR MEDICINE
A biosimilar medicine is a biological medicine which is similar to another biological medicine that has already been authorized for use. Biosimilar medicines are commonly known as biological generic medicines. The existing biological medicine is known as the 'reference medicinal product'. Biosimilars may only be marketed

after the patent for the reference medicinal product has expired, although they may be developed earlier. A biosimilar medicine and its reference medicinal product are expected to have the same safety and efficacy profile.
Biosimilar medicines are developed to have the same mechanism of action, and to treat the same diseases as the reference medicinal product. Standards of the EU Good Manufacturing Practice (GMP) apply to the manufacture of biosimilar medicines in the same way as for any other biological medicinal product. Biosimilar medicines may offer a less costly alternative to existing biological medicinal products that have lost their exclusivity rights.

BIOTECHNOLOGY
Any technological application of living systems, biological processes or organisms, to develop or make useful products or new technologies.

BIOTRANSFORMATION
Biotransformation is the process whereby a substance is changed (transformed) from one chemical to another by a chemical reaction within the body. Biotransformation is vital to survival because absorbed nutrients (food, oxygen, etc.) are transformed into substances required for normal body functions. For some pharmaceuticals, it is a metabolite that is therapeutic and not the active pharmaceutical ingredient of a medicine itself.

BLINDING
Blinding is a way of making sure that the people involved in a research study, such as the participants in clinical trials, do not know which trial arm they are assigned to. For example, in a trial with one treatment arm and one placebo arm, blinding means that the participants do not know if they are receiving the treatment or the placebo.
Blinding is used to remove bias that can be caused intentionally or unintentionally if participants or the research team are aware of which trial group participants are in.
The term 'single-blind' is used to describe studies where the participants are unaware of which arm they are in, but the research team does know. In a double-blind trial, both the research team and participants do not know which participant is assigned to which arm.
A blind trial is the opposite of an open or open-label trial.

BOLUS INSULIN
Bolus insulin is the burst of insulin release in the blood stream when eating. The high levels of insulin help the glucose get out of the blood stream and be stored for future use.

BRANDED MEDICINES
Branded medicines are medicines which have a name given to them by a company for the purpose of advertising. The names of branded medicines are different from the International Nonproprietary Name (INN), also known as the generic name. Branded medicines may be the original medicine developed by a company or several companies may make the same generic medicine, to which each company gives its own brand name.

BUDGET IMPACT
Costs within a particular timeframe and related to a particular healthcare budget rather than a country's overall budget. This assumes robust data on epidemiology and treatment patterns, along with assumptions of uptake and displacement of current treatments.

C

CANDIDATE DRUG
In the medicines development process, this is the compound among several, which meets criteria in efficacy and safety in order to be used in clinical trials with humans. Broad information on the mechanism of action and pharmacology has to be available for a candidate drug.

CANDIDATE GENE
A candidate gene is any DNA sequence (gene) in a chromosome considered likely to cause a disease. The gene may be a candidate because it is located in a particular chromosome region involved in the disease, or its protein product is suspected to be the cause of the disease. Candidate genes have been used to identify genetic risk factors for complex disorders such as alcoholism.
These studies, called the candidate gene approach, test the effects of variants of a candidate gene in members of an affected family, or in unrelated cases and controls. The candidate gene approach is useful for quickly determining the association of a genetic variant with a disorder. However, this approach is limited by how much is known about the biology of the disease being investigated.

CARCINOGENICITY
The ability of a substance to cause cancer or increase the risk of cancer development.

CARCINOGENICITY STUDIES
Studies that use animal models to evaluate the carcinogenic potential of pharmaceuticals. They are also used to test chemicals and food additives. The objectives of carcinogenicity studies are to identify a tumorigenic potential in animals and to assess the relevant risk in humans. Any cause for concern derived from laboratory investigations, animal toxicology studies, and data in humans may lead to a need for carcinogenicity studies. The fundamental considerations in assessing the need for carcinogenicity studies are the maximum duration of patient treatment and any perceived cause for concern arising from other investigations.

CASE CONTROL STUDIES
A case control study is one that compares two groups retrospectively.
For example, people who developed a disease might be compared with a group of people who have not. The researcher will look at whether there is any difference in the two groups in their previous exposure to possible risk factors. This kind of study is useful when studying risk factors for rare diseases, and is often used to create new hypotheses which can then be tested.

CASE REPORT FORM (CRF)
A case report form (CRF) is a paper or electronic data (eCRF) entry form used in clinical trials. It is used by sites taking part in clinical trials (such as hospitals) to collect data about each trial participant. All the data on each individual taking part in a clinical trial, including information on adverse events, are held in the case report form.
A CRF is developed specifically for each clinical trial so that all the data needed to answer the research question is captured. The organization running the trial is responsible for designing a case report form in line with the protocol of the trial. They must also monitor and audit the data that is collected to ensure it is complete and accurate.
Personal data such as, the patients' names, medical record numbers, and any other identifying information are usually not disclosed in the CRF's. Each patient is instead given a unique identifier.

CAUSAL RELATIONSHIP
Is the relation between an event (the cause) and a second event (the effect), where the effect is a direct consequence of the cause.

CENTRALISED PROCEDURE
The centralized procedure is a process for obtaining marketing authorization for a medicine in the EU. The European Medicines Agency (EMA) oversees the centralized authorization procedure for human and veterinary medicines. This procedure results in a single marketing authorization, granted by the European

Commission, which allows a medicine to be marketed in all EEA (European Economic Area) countries (EU member states and the three EEA EFTA States: Iceland, Liechtenstein, and Norway).

CHRONIC CONDITION
A chronic condition is a long-lasting disease that can be controlled but not cured. The term chronic is usually applied when the course of the disease lasts for more than three months.
Common chronic diseases include asthma, chronic obstructive pulmonary disease (COPD), cancer, and diabetes. In certain diseases or conditions, prevention is effective in reducing the possible development of the condition or its effect. Early diagnosis and timely treatment can help to reduce serious effects of the condition.

CLASS EFFECT
Class effect refers to the similar outcomes, therapeutic effects and similar adverse effects of two or more medicines. All products within a class are assumed to be closely related in three concepts: a similar chemical structure, mechanism of action, and pharmacological effects.

CLASSIFICATION OF A MEDICINAL PRODUCT
In the EU there are two classifications of medicinal products for human use:
- medicinal products subject to medical prescription
- medicinal products not subject to medical prescription
- further subcategories may exist on a national level

CLEARANCE
Clearance is a term in pharmacokinetics which describes the volume of plasma that is completely cleared of a substance per unit time. The usual units are mL/min. The total body clearance will be equal to the renal (kidney) clearance + hepatic (liver) clearance + lung clearance although for many medicines the clearance is simply considered as the renal excretion ability.

CLINICAL DEVELOPMENT
Clinical development is one step in the process of bringing new medicines or treatments to the market. Based on non-clinical research (microorganisms/animals), it refers to clinical trials, which are done in people. They follow different phases designated as Phase I, II, III (and IV after marketing authorisation).

CLINICAL DOSSIER
A comprehensive collection of data, documents, and information compiled to support the regulatory approval of a drug or therapy.

CLINICAL EFFECTIVENESS
As a component of a dossier submitted for health technology assessment (HTA), clinical effectiveness is a measure of how well a particular treatment works in the practice of medicine. It depends on the application of the best knowledge derived from research, clinical experience, and patient preferences.

CLINICAL EFFICACY
Clinical efficacy indicates a positive therapeutic effect. If efficacy is established, an intervention is likely to be at least as good as other available interventions to which it will have been compared. When talking in terms of efficacy versus effectiveness, efficacy measures how well a treatment works in clinical trials or laboratory studies. Effectiveness, on the other hand, relates to how well a treatment works in the practice of medicine.

CLINICAL PHARMACOLOGY
In relation to clinical development, pharmacology deals with the effects of compounds (medicines in development) in healthy volunteers and in patients. It usually includes pharmacodynamics and pharmacokinetics. In the evaluation process the action and adverse effects of compounds can be measured and compared.

CLINICAL PHASE
The clinical phase of medicine development is the one involving humans, and is different from the 'non-clinical' or 'pre-clinical phase' in which studies are performed in labs or in animals (such as for pharmacology/toxicology analysis). Clinical studies are conducted in four steps, called 'phases' - each designed to answer separate research questions:

CLINICAL PRACTICE
Clinical practice is the treatment and management of patients by healthcare professionals supported by clinical-based evidence. There are clinical practice guidelines that have been designed to assist health professionals and patients in decisions about appropriate health care for specific circumstances.

CLINICAL STUDY
A clinical study is a scientific investigation in which participants receive a health-related intervention, such as a medicine, in order to learn about (discover or verify) how it works and interacts with the body (clinical, pharmacological, pharmacodynamic, and pharmacokinetic effects), or to identify any adverse reaction in order to understand the safety of and/or how well the medicine works (efficacy).
Previously, the terms clinical study and clinical trial were used synonymously. Refer to Regulation 2014/536 for more information.

CLINICAL STUDY REPORT
A clinical study report is a document containing extensive detail about the plan, methods and conduct of the study so that it is clear how the study was carried out. This report should provide a clear explanation of how the design features of the study were chosen and include results of the trial. A clinical study report should also provide enough individual patient data, to allow the key analyses of data to be repeated, should the regulatory authorities wish to do so. It is a central part of any application for a new medicine to receive marketing authorization, and it must meet the requirements of the regulatory authority that has to assess the application.

CLINICAL TRIAL (CT)
A clinical trial is a clinical study in which participants are assigned according to a pre-defined therapeutic strategy or plan (protocol) to receive a health-related intervention, such as a medicine, in order to investigate its effects on health outcomes, usually compared to another (or sometimes no) treatment.
Clinical trials are used to evaluate clinical practices that do not fall within the current practices of a country, or to evaluate a new medicine (investigational medicinal product).
Clinical trials are used to generate data on the safety and efficacy of the intervention. Clinical trials are conducted only after a regulatory authority approval and ethics committee review. Clinical trials are often characterized in Phases from I (first-in-human), II (exploratory), III (confirmatory) to IV (post approval).
Previously, the terms clinical study and clinical trial were used synonymously. Refer to Regulation 2014/536 for more information.

CLINICAL TRIAL AUTHORIZATION (CTA)
Before a clinical trial can start, the sponsor must apply for and be given clinical trial authorization (CTA). Each European country has its own regulatory authority that assesses applications for clinical trial authorizations.
For clinical trials that will take place in more than one European country, there is a Voluntary Harmonization Procedure which allows one application to be submitted to the authorities in all the relevant countries.
As well as clinical trial authorization, a positive opinion from an ethics committee (or institutional review board) is needed before a clinical trial can go ahead.

CLINICALTRIALS.GOV
ClinicalTrials.gov is an online resource that provides information about clinical studies on a wide range of diseases. It includes information on whether the studies are recruiting patients, and a summary of the results of studies once they have finished.
The resource can be found at https://clinicaltrials.gov.
Studies can be searched for by disease or by country. Although it is funded by the US government, it includes studies based around the world. The resource is aimed at patients and their families, healthcare professionals, researchers and the public. The website is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH).

CLINICIAN-REPORTED OUTCOME
A type of outcome assessment determined by a trained health-care professional after observation of a patient's health condition.

CLINICAL RESEARCH ASSOCIATE (CRA)
A professional responsible for monitoring and managing clinical trials to ensure compliance with protocols, regulations, and ethical standards.

CLINICAL TEAM
A group of healthcare professionals involved in conducting clinical trials or providing medical care to patients.

COHORT STUDIES
Cohort studies are used to study how common diseases are, their causes, and their prognoses. Cohorts are groups of people who are selected on the basis of certain characteristics. For example, if exposure to a risk factor such as cigarette smoke is suspected to cause a disease, a cohort can be selected in which one group has been exposed and another group has not. Both groups are then studied for signs or symptoms of disease. Cohort studies can be prospective (cohorts are identified before any signs of disease and are followed up over time) or retrospective (data is used that has already been collected, possibly over a long period of time).
Cohort studies are a kind of observational study, in which the researcher does not perform any intervention (such as administering a medicine).
Cohort studies are useful when it would be unethical to carry out a randomized controlled trial (RCT). For example, deliberately exposing people to cigarette smoke or asbestos would be unethical and therefore cannot be done.

COMBINED ADVANCED-THERAPY MEDICINES
Combined advanced-therapy medicines are medical products based on the combination of genes (gene therapy), cell therapy (cell therapy) or tissues (tissue engineering) with one or more medical devices as an integral part of the medicine.

COMPASSIONATE USE
Method of providing an unlicensed medicine prior to final approval by a regulatory (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 medicine or therapy.

COMPOUND
Two or more elements or molecules which are chemically bound to each other. The term compound is often used to refer to a medicine which is being developed.

CONCOMITANT
Something that exists or occurs at the same time as something else. It can be a natural event, but in medicine is used when referring to:
• concomitant medication: two or more medicines are given at the same time when treating diseases
• concomitant disease: a second disease (or more) is present at the same time as the primary disease (or secondary symptoms occur with a main symptom)

CONFIDENCE INTERVAL
A confidence interval is an estimated range of values in which all data (results) are likely to lie. For a given treatment effect measured in a trial on a sample of a population, the confidence interval can be calculated to give a 'best estimate' range of the treatment effect that will be seen in the whole population.
The likelihood that the confidence interval will contain the value is called the confidence level. Traditionally, confidence levels are set at 95% or 99%. This means that researchers are 95% (or 99%) certain that the measured effect lies within the true range.
For example, instead of estimating the mean age of a population as 15 years, researchers say that the mean age is between 14 and 16. This confidence interval contains the true value being estimated.

CONFIRMATORY STUDIES
These are studies conducted in Phase III of the clinical development of a medicine. They aim to confirm the efficacy and safety in a large patient population. They can involve thousands of patients, can be run in many countries, require a huge amount of expertise to be run effectively, and are therefore resource intense and very time consuming. They are the largest, most complicated, and most expensive part of the development of a medicine.

CONFOUNDING VARIABLE

A confounding variable is something, other than the treatment being studied, that can affect the measured outcome of a trial. For example, imagine that a medicine to prevent the common cold is tested by administering it to 1,000 men, while a placebo is administered to a group of 1,000 women. The trial results show that far fewer men caught a cold during the trial period. It would not, however, be possible to conclude that the medicine had an effect because all of the placebo group were women, and therefore gender is a confounding factor. The trial results could have a plausible alternative explanation - for example, that women are more susceptible to the cold viruses circulating at the time of the study.
Well-designed trials take account of potential confounding variables and allow the elimination of plausible alternative explanations for study findings. In the example given above, men and women could be randomly assigned to the intervention and placebo groups to remove gender as a confounding variable.

CONTRACT RESEARCH ORGANIZATION (CRO)

A contract research organization (CRO) is an independent organization that provides support into the medicines development process. Typically, a CRO will organize and conduct clinical trials to test an investigational medicinal product in humans.

COST EFFECTIVENESS

In the context of pharmacoeconomic, cost effectiveness is studied by looking at the results of different interventions by measuring a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, or cases detected).
Alternative interventions are then compared in terms of cost per (natural) unit of effectiveness in order to assess how it provides value for money. This economic evaluation helps decision-makers to determine where to allocate limited healthcare resources.

Cost effectiveness, however, is only one of a number of criteria that should be used to determine whether or not interventions are made available. Other issues, such as equity, needs, and priorities should also be part of the decision-making process.

C-PEPTIDE

C-peptide is a protein released by β cells (beta cells) during the production of insulin. Proinsulin is divided into insulin and C-peptide. Since C-peptide is secreted in equal amounts to insulin, measuring C-peptide levels can provide insight into the body's insulin production.

CRITERIA FOR 'GO/NO-GO' DECISIONS

Compounds under investigation as potential new medicines must meet certain criteria, at each stage of development, in order to progress further. These criteria need to be agreed upon by the medicines developers. A go decision means that the compound meets the criteria, and will be advanced to the next development step. Failure to meet the criteria will lead to a no-go decision and the medicine development will stop.

CROSS-OVER STUDY

A study design where participants receive multiple treatments or interventions in a sequential order, with each participant acting as their own control. For example, participants may receive one treatment for a certain period, then switch to another treatment for a subsequent period. The key feature is that each participant serves as their own control, allowing for more efficient comparison of treatments while reducing the impact of individual differences.

CURATIVE TREATMENT

Curative treatment is a treatment aimed at curing or eliminating a disease or condition.

D

DATA AND SAFETY MONITORING BOARD (DSMB)
A Data and Safety Monitoring Board (DSMB) is an independent group of experts set up to protect patient safety during a clinical trial. This board periodically reviews clinical study data (and they have access to unblinded data in case of blinded studies), incidental event reporting, and clinical study performance. The DSMB provides independent advice to ensure participants are not exposed to undue risks, and make recommendations concerning the continuation, modification, or termination of a trial.

DATA EXCLUSIVITY
Data exclusivity refers to the period during which the data of the original marketing authorization holder is protected. It is the time during which another company cannot use the originator's data in support of another marketing authorization application, i.e.: generics, hybrids, biosimilars. Therefore, competent authorities may not accept such an application during this period of time. In Europe, this protection period lasts for a minimum of eight years and is intended to incentivize innovation.

DATA MANIPULATION
Data manipulation is the process of taking data and manipulating (reformatting) it to be easier to read or better organized. For example, a list of data entries could be organized in alphabetical order, making it easier to view and find information.
However, these practices should be used carefully as they can lead to the selective incorrect reporting of data or creation of false results (see bias).

DATA MERGING
Data merging is a process that involves combining data from different sources, and providing users with a single view of these data.
For example:

- data from different hospital sites within a clinical trial will be combined for analysis
- data generated from entirely separate scientific studies might be combined if this will provide a better data set for analysis

DATA MINING
Data mining is the practice of searching through existing large sets of data to find useful patterns or trends. Data mining can generate new hypotheses or new ideas for diagnosing, preventing, or treating diseases. It can, for example, lead to predictions for individual responses to medicines, or help with the design of completely new medicines.
The pharmaceutical industry uses sophisticated computer-driven data-mining techniques in an effort to extract information from the large amounts of chemical, biological, and clinical data available.
Data can be mined from clinical trial data sets, data from biobanks, or any other data set that is accessible " for example, data sets held by public research organizations or insurance companies.

DECENTRALIZED PROCEDURE
The decentralized procedure is a process for authorizing medicines in more than one European Union member state at the same time.

DECLARATION OF HELSINKI
A set of ethical principles regarding human experimentation developed by the World Medical Association (WMA). It was first adopted in 1964 and has since been revised multiple times. The Declaration of Helsinki provides guidance on the ethical conduct of medical research involving human subjects, emphasizing principles such as informed consent, protection of vulnerable populations, and respect for participant autonomy and confidentiality.

DEGRADANTS
Chemical products formed from the breakdown of a medicine due to for example light, temperature, water, reaction with non-active substances, or container and closure systems, etc.

DELIVERY DEVICE
A device used for the delivery of a medicine or therapeutic agent via a specific route of administration (e.g. inhaler, dermal patch or infusion pump).

DELIVERY SYSTEM
Medicine delivery systems encompass four main related aspects:

- Routes of delivery (ways in which the medications can be taken, such as orally, by injection, by inhalation, etc.).
- Delivery vehicles (dosage forms such as pills or slow-release granules).
- Chemical/biological properties of the active substance of the medicine (the cargo).
- Targeting strategies (delivery methods that deliver medicines to specific organs, tissues, tumors or structures inside of cells).

DEVELOPMENT
The process of creating or improving drugs, therapies, or medical technologies.

DEVELOPMENT SAFETY UPDATE REPORT
The Development Safety Update Report is an annual review of safety information during clinical trials of a medicine under investigation whether or not it is marketed. The main objectives of a Development Safety Update Report is to:

- Summarize the current understanding and management of identified and potential risks.
- Describe new safety issues that could have an impact on the protection of clinical trial participants.
- Examine whether any new safety information is in line with previous knowledge of the product's safety.
- Provide an update on the status of the clinical investigation/development program and study results.
- Developmental and reproductive toxicity
- Developmental and reproductive toxicity (DART) is studied in animals to test chemical substances or medicines that might interfere with normal reproduction. This includes adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring (child).

DIRECTIVE
An EU Directive is a form of legislation that is directed at the member states of the EU. Directives set out a goal or policy which needs to be achieved by the member states. A directive shall be binding upon each member state to which it is addressed, but shall leave to the national authorities the choice of form and methods. The member states are required to make the appropriate changes to their national legislation to implement the Directive. Normally this must be done within two years.
A wide range of issues is dealt with by directives, including some aspects of health and social policy.

DISABILITY-ADJUSTED LIFE YEAR (DALY)
The disability-adjusted life year (DALY) is a measure used in health economics. It represents the 'burden' of a disease, expressed as the number of years lost due to ill-health, disability, or early death. One DALY can be thought of as one lost year of 'healthy' life.

The total of DALYs across a population can also be thought of as a measurement of the gap between the population's current health status and an ideal situation in which every person enjoys perfect health into old age.

DISCOVERY STAGE
The initial phase of drug development where potential drug candidates are identified and characterized through research and experimentation.

DISEASE BURDEN
Also known as unmet need or therapeutic need. It may be a measure of the number of people affected by a particular disease for whom current treatments are inadequate. It may include the number of new diagnoses

of a disease, or the costs to society or a government representing those affected. It may also include more qualitative aspects about the burden of disease and current treatments available to patients.

DISEASE MODIFYING THERAPY (DMT)
Treatment designed to alter the course or progression of a disease, rather than just alleviating symptoms.

DOSAGE
Dosage is a measured and specific amount of a medicine, with number, and frequency of doses over a specified period of time or prescribed intervals.

DOSAGE FORMS
Dosage forms of a medicine are the means (or the form) by which drug molecules are delivered to sites of action within the body. There are several types of dosage form, depending on the method/route of delivery of the medicine. These include for instance pills, capsules, syrups, suppositories and solutions for injection. Typically this involves a mixture of the active substance(s) and non-active substances (excipients).

DOSAGE REGIMEN
The dosage regimen is the schedule of doses of a medicine, including the time between doses, the duration of treatment and the amount to be taken each time. Dosage regimens also include how a medicine is to be taken, and in what formulation (dosage form).

DOSE
A dose is a single, measured amount of a medicine to be taken at one time. This can be expressed as the forms (e.g. 1 capsule, 1 suppository), weight (e.g. 250 mg), volume (e.g. 10 mL, 2 drops), or some other quantity (e.g. 2 puffs).

DOSE-RANGING
In a dose-ranging study different doses of a medicine are tested against each other to establish which dose works best and/or is least harmful.

DOSSIER
A dossier refers to a collection of documents or information compiled and organized for a specific purpose, such as regulatory submission or evaluation. In the context of pharmaceuticals, a dossier typically contains comprehensive data on a drug or medical product, including information on its development, manufacturing processes, preclinical and clinical trial results, safety profiles, and proposed labeling. Dossiers are submitted to regulatory authorities as part of the approval process for marketing authorization or to support other regulatory activities.

DOUBLE BLIND
Double blinding is a method used in clinical trials to reduce the risk of bias, which can be caused intentionally or unintentionally when trial participants and/or researchers are aware of which participants are receiving which treatment (or placebo).
For example, in a trial with one treatment group and one placebo group, blinding means that the participants do not know which group they have been assigned to. In a double-blind trial, neither the research team nor the participants know which participant is assigned to which group.

DRUG CANDIDATE
In medicines development, the drug candidate is the molecule among several that has been shown to have sufficient target selectivity and potency, and favorable medicine-like properties and justifies further development. It will then be subjected to a new series of tests, and non-clinical studies and clinical trials. At this stage it is not yet a medicine.

DRUG DEVELOPMENT
Drug development is the process of bringing a new medicine to the market once a drug candidate (lead compound) has been identified in drug discovery. It includes non-clinical tests on microorganisms and animals, application to the regulatory authority to initiate clinical trials on humans, and may include the step of obtaining regulatory approval with a Marketing Authorization Application to market the drug. It is also known as medicines development. EUPATI and INNODIA use the term medicines development throughout their texts.

DRUG DISTRIBUTION
The process by which a medicine is distributed from one location to another within the body. See also pharmacokinetics.

DRUG SUBSTANCE
An ingredient intended to exert pharmacologic action or other direct effect in the diagnosis, cure, mitigation, or prevention of disease or to affect any function of the body. Along with other ingredients (excipients,) it is used to formulate a medicinal product.

DRUG TOLERANCE
Tolerance of a medicine may be considered as the ability of the body to endure a certain dose of a medicine. In contrast, drug tolerance refers to a decreasing response to repeated constant doses of a medicine, or the need for increasing doses to maintain a constant response. Drug tolerance can lead to physical (physiological) or emotional dependence, which is an adaptive state associated with a withdrawal syndrome on cessation of repeated exposure to a medicine.

DYSGLYCEMIA
Abnormal blood glucose levels, which may include hyperglycemia (high blood sugar) or hypoglycemia (low blood sugar).

E

EFFECTIVENESS
The capability of a medicine to produce a desired or expected effect in the real world clinical setting. When talking in terms of efficacy vs. effectiveness, effectiveness relates to how well a treatment works in the practice of medicine, as opposed to efficacy, which measures how well a treatment works in clinical trials or laboratory studies.

EFFICACY
Efficacy refers to the ability of a medicine to provide a beneficial effect (a positive benefit/risk ratio) when studied in a clinical trial. When talking in terms of efficacy vs. effectiveness, effectiveness relates to how well a treatment works in the real-world practice of medicine, as opposed to efficacy, which measures how well a treatment works in clinical trials or laboratory studies.

EFFICIENCY
In the context of health economics, efficiency of a medicine is a measure of its ability to provide a beneficial effect against its costs to individuals or society. The most efficacious treatment may not be the most efficient (cost-effective) option, for example making it unaffordable for the patients or the health system to implement.

ELIGIBILITY
Eligibility in medicines development usually refers to the requirements that participants must meet in order for them to have the possibility of being selected to participate in a clinical trial. The requirements (criteria) will typically contain not only elements which allow participation (inclusion criteria) but also details of what will prevent someone from participating (exclusion criteria).

ENDOCRINE THERAPY
Endocrine therapy, or hormone therapy, is a therapy that adds, blocks, or removes hormones in order to treat a disease. For certain conditions (such as diabetes or menopause), hormones are given to adjust low hormone levels. Hormones can also be given to block the production of natural hormones and to slow or stop the growth of certain cancers (such as prostate and breast cancer).

ENDOTYPE
Subpopulations, with various characteristics which behave differently in terms of onset of a disease, severity and also response to treatment.

ENDPOINT
The endpoint of a clinical trial is a pre-defined event: for instance, the occurrence of a disease, the occurrence of a symptom, or a particular laboratory result. Once someone reaches the endpoint, they are generally excluded from further research in the trial.

Endpoints can be hard (objective) or soft (subjective). In some cases they can be replaced by surrogate endpoints. The endpoints used in a trial must be defined and documented as part of the trial protocol.

EPIGENETICS
Epigenetics is the study of changes in gene activity (expression) that do not involve changes in the underlying DNA sequence (genotype). Epigenetic changes are a regular and natural occurrence, but they can also be influenced by several factors including age, environment/lifestyle, and disease state through mechanisms that switch genes on or off.

EPIGENOMICS
Epigenomics is the study of the complete set of epigenetic modifications on the genetic material of a cell, known as the epigenome. The epigenome marks the genome in two main ways, both of which play a role in turning genes on or off.

In epigenomics, researchers try to chart the locations and understand the functions of all the chemical tags that mark the genome. Epigenomic maps may someday help doctors make diagnoses and tailor a patient's response to therapies.

EQUITY CONSIDERATIONS
An assessment of how adoption of the new therapy might impact measures of fairness within the health system. For example, will the therapy lead to more benefits for people who are socially or economically disadvantaged?

ETHICAL PRINCIPLES
Ethical principles exist both to protect the research participants and to ensure the integrity of the research. There are various codes and regulations which guide ethical research today, including the Declaration of Helsinki, although a number of common principles exist.
The World Medical Association (WMA) developed the **Declaration of Helsinki** as a statement of ethical principles specifically for medical research involving human subjects. It emphasizes the procedures required to ensure subject safety in clinical trials including informed consent and review by research ethics committees.

ETHICS COMMITTEE (EC)
An Ethics Committee (EC) is an independent body made up of a range of individuals including medical or scientific professionals and non-medical or non-scientific members (e.g. patients or lay members). An EC may operate within an institution, or it may be national, or supranational or private.
ECs have a responsibility to ensure the protection of the rights, safety and wellbeing of research participants, as well as assuring the public of that protection. It operates, among other things, expressing an opinion on the clinical trial protocol, the suitability of the investigators involved in the trial, the adequacy of facilities, and on the methods and documents to be used to inform trial participants and obtain their informed consent. A trial should only begin when a favorable opinion by an EC has been given.

EU REGULATION
A regulation is a written rule or law. European regulations are binding legislative acts. They must be applied in their entirety across the EU simultaneously from the date agreed. Regulations can be distinguished from European directives which are legislative acts that set out a goal that all EU countries must achieve. However, it is up to the individual countries to devise their own laws on how to reach these goals. Directives need to be converted into national law before they are enforceable.

EUNETHTA
The European network for Health Technology Assessment was established to create a network for HTA across Europe, developing a framework (HTA Core Model®) by which a technology (for example a new medicine) can be assessed. It facilitates efficient use of resources, creating a sustainable system of knowledge, and promoting good practice in HTA methods and processes. The network connects public national HTA bodies, research institutions and health ministries, to exchange information and to support policy decisions by member states.

EUROBIOBANK
The EuroBioBank network is the first operating network of biobanks in Europe providing human DNA, cell, and tissue samples as a service to the scientific community conducting research on rare diseases. It was established by patients and researchers.
A biobank is a large, organized collection of samples, usually human, used for research. Biobanks catalogue and store samples using genetic, clinical, and other characteristics such as age, gender, blood type, and ethnicity. Some samples are also categorized according to environmental factors, such as whether the donor had been exposed to some substance that can affect health. Biobanks play a crucial role in biomedical research, such as in genomics and personalized medicine. Researchers access biobanks when they need samples with similar characteristics for their research studies.

EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)
A European Public Assessment Report (EPAR) is an assessment produced for all medicines where marketing authorization is sought through the centralized procedure at the European Medicines Agency (EMA). It is a series of documents, and includes:

- a lay summary
- details about the marketing authorization holder

- product information (such as the package leaflet and summary of product characteristics)
- details about the assessment carried out at EMA
- EPARs are published on the EMA's website once the European Commission has issued a decision regarding a marketing authorization

EVIDENCE-BASED MEDICINE (EBM)
Evidence-based medicine (EBM) applies the scientific method to medical practice, using techniques from science, engineering, and statistics - such as the meta-analysis of scientific literature, benefit-risk analysis, and randomized controlled trials. One of the goals of evidence-based medicine is that healthcare professionals should make 'conscientious, explicit, and judicious use of current best evidence' in their everyday practice.

EXCIPIENT
Pharmaceutical excipients are natural or synthetic substances combined with the active substance in a dosage form. Excipients assist the drug or active substances to be better metabolized or administered. They protect, support or enhance stability or facilitate absorption of the medicine in the body. They may also assist in product identification (e.g. by color of a tablet/capsule).

EXCLUSION CRITERIA
Exclusion criteria are characteristics that exclude people from taking part in a trial.
For example, depending on the requirements of the trial, exclusion criteria might include age, gender, type or stage of disease, and the presence or absence of other medical conditions. For a trial studying an anti-venom (snake bite) medicine, some of the criteria that would exclude an individual from taking part might be:

- Pregnancy
- Aged under 12 or over 70
- Previously received an anti-venom medicine
- Medical history includes wheezing, high blood pressure, heart disease
- Known adverse reaction to adrenaline.

Exclusion criteria (and inclusion criteria) are an important part of a trial protocol. If they are properly defined, exclusion and inclusion criteria will increase the chances of a trial producing reliable results. They also protect participants from harm and help avoid exploitation of vulnerable people (such as those unable to provide informed consent).
The reason for choosing the exclusion criteria should be documented with the trial protocol. Exclusion of certain groups can affect how realistic it is to generalize the trial results to the relevant patient population (external validity). This should be considered by researchers when they are designing a trial, and unnecessary exclusions should be avoided.

EXPANSION COHORT
A group of participants added to a clinical trial to further evaluate the safety and efficacy of a drug or therapy, often based on promising results from earlier stages.

EXPLORATORY TRIALS
Exploratory trials are developed to select compounds or targeted medicines or approaches based on human data rather than animal data. They are conducted early in Phase I of the clinical development process, which involve limited human exposure, have no therapeutic intent, and are not intended to define a maximum tolerated dose.

EXTRACTABLES
Compounds that can be extracted from plastic or coatings of a container or closure system in direct contact with an active substance or medicinal product. Regulatory guidelines stipulate that an extractable profile should be determined for all materials in contact with the medicine or patient directly to ensure medicine safety.

F

FASTING PLASMA GLUCOSE
The concentration of glucose in the blood after an overnight fast, used as a diagnostic criterion for diabetes.

FDA
Food and Drug Administration. USA National Competent Authority. http://www.fda.gov/

FORMULATION
A formulation is a mixture of different chemical substances prepared according to a specific method to create a medicinal product.

FRAUD
Fraud is an intentional act of deception. An example of fraud within a research setting might be a deliberate attempt to fabricate data or present data in a misleading way. Fraud does not include honest errors or poor research processes, unless it is done with an intention to deceive. In research, fraud can impact the sponsor financially, have severe consequences for a study's credibility, and could even lead to patients accessing ineffective or harmful treatments.

FUTILITY
Futility is the inability of a clinical trial to achieve its objectives.
Problems such as difficulty recruiting enough patients can mean that a trial will not give a result that can be properly statistically analyzed. If such problems are discovered during the trial, it may be appropriate to stop the trial early. This kind of calculation is known as a futility assessment, and is one kind of interim analysis.
Stopping a trial early because it is unlikely to achieve a statistically reliable result is ethically appropriate because it prevents exposure of patients unnecessarily to treatments or other interventions. It can also save time and therefore costs.

G

GAMETE
A cell that fuses with another cell during conception in organisms that reproduce sexually. In species that produce two morphologically distinct types of gametes, and in which each individual produces only one type, a female gamete is called an ovum (or egg), and a male gamete is called a sperm.

GENERAL DATA PROTECTION REGULATION (GDPR)
EU General Data Protection Regulation (GDPR) replaces the Data Protection Directive 95/46/EC and was designed to harmonize data privacy laws across Europe, to protect and empower all EU citizens data privacy, and to reshape the way organizations across the region approach data privacy. The final Regulation provides more rights to citizens to be better informed about the use made of their personal data, and gives clearer responsibilities to people and entities using personal data.
GDPR covers patients' fundamental right to protection of their health data and is an important issue in diverse contexts such as healthcare, including care given through eHealth or in a cross-border healthcare context, and research (clinical trials, clinical investigations, epidemiological research, patient registries, etc.). Health and genetic data belong to the category of sensitive data, and benefit from additional protection.
Refer to Regulation (EU) 2016/679 for more information.

GENE MUTATION
A gene mutation is a permanent alteration in the DNA sequence that makes up a gene. Mutations range in size, affecting from a single DNA building block (base pair) to a large segment of a chromosome with multiple genes. Gene mutations can be classified in two ways:
• Germ-line mutations are inherited from a parent and are present throughout a person's life in every cell in the body. These mutations are present in the parent's egg or sperm cells, and are transmitted as hereditary mutations.
• Somatic mutations occur at some point during a person's life only in certain cells, not in every cell in the body. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. These acquired mutations cannot be passed on to the next generation.

GENE THERAPY
Gene therapy is an experimental technique that replaces a faulty gene in a cell, or adds a new gene to cure or prevent disease. In the future, this technique may allow doctors to treat a disorder instead of using medicines or surgery. Researchers are testing several approaches to gene therapy, including replacing a mutated gene that causes disease, deactivating a mutated gene that is not properly functioning, or introducing a new gene into the body to help fight a disease.
Although gene therapy is a promising treatment option for a number of diseases, the technique is still under study to make sure that it will be safe and effective. Gene therapy is currently only being tested for the treatment of diseases that have no other cures.

GENETIC RISK
The likelihood of developing a disease or condition based on one's genetic makeup.

GENETIC PREDISPOSITION
Increased likelihood of developing a disease or condition due to genetic factors.

GENERIC MEDICINE
A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorized, called the 'reference medicine'.
A generic medicine contains the same active substances as the reference medicine, and it is used at the same doses to treat the same diseases. However, a generic medicine's inactive ingredients, name, appearance, and packaging can be different from the reference medicine's.
Generic medicines are manufactured according to the same quality standards as all other medicines. A company can only develop a generic medicine for marketing once the period of exclusivity on the reference medicine has expired. This is usually 10 years from the date of first authorization.

GENETICALLY MODIFIED ORGANISM (GMO)

A genetically modified organism (GMO) is an organism whose genetic material has been altered in the laboratory. Genetic modifications are made to produce certain traits (such as disease resistance in crops) or to cause the organism to produce specific biological products (for example, bacteria have been altered in order to produce insulin for diabetes treatment, and plants have been altered to make antibodies and blood-clotting factors).
GMOs are used in the production of medicines, and in new forms of medicines such as gene therapy.
Genetic modification is also a useful tool for scientists in many areas of research, including those who study the mechanisms of human and other diseases.

GENOME

The genome is an organism's complete set of genetic instructions. Each genome contains all of the information needed to build that organism and allow it to grow and develop. The genome includes both the genes and the non-coding sequences of the DNA/RNA. The human genome contains about 35,000 genes.
The Human Genome Project, completed in 2003, was an international effort to identify all the genes in human DNA, and to determine the sequences of the 3 billion base pairs of DNA. It took 13 years.
Genome research has helped diagnose diseases and find genetic markers for certain diseases.

GENOMIC MARKER

A genomic marker (or genetic marker) is a specific gene or DNA sequence that is associated with a known characteristic. They are used to study the relationship between diseases and genetics. A genetic marker can serve as a flag for another gene. It must be on the same chromosome and near enough to the other gene that the two genes are genetically linked and are usually inherited together.

GENOMIC TECHNOLOGIES

Genomic technologies are those new methods, technologies, and instruments used to study and manipulate the genome.

GENOMICS

Genomics is the branch of biology that studies the entire genome of an organism by sequencing, assembling, and analyzing the function and structure of its DNA. Advances in genomics have allowed great progress to be made in understanding diverse illnesses.
Genomics research can develop more effective therapeutic strategies, and better decision-making tools for patients and healthcare providers.

GENOTOXICITY STUDY

A genotoxicity study is designed to detect compounds that cause genetic damage either directly or indirectly in cells exposed to the toxic substrates. Genotoxicity studies may be performed in vitro or in vivo.
Compounds which are positive in tests that detect such damage have the potential to cause cancer and/or heritable defects. No single test is capable of detecting all relevant genotoxic agents therefore, the usual approach is to carry out a battery of tests that are complementary rather than representing different levels of hierarchy.
A standard study battery has the following tests:

- A test for gene mutation in bacteria
- An in vitro test with cytogenetic (concerned with the study of the structure and function of the cell) evaluation of chromosomal damage with mammalian cells
- An in vivo test for chromosomal damage using rodent hematopoietic (blood or blood cell forming) cells

GENOTOXIN

A chemical or other agent that provokes a harmful change in a person's genetic material regardless of the mechanism by which the change is induced. A genotoxin can cause mutations in DNA (a mutagen), it can trigger cancer (a carcinogen), or it can cause a birth defect (a teratogen).

GENOTYPE

The genotype is an individual's collection of genes, including which genetic variants they have. It is the entire

complex of genes inherited from both parents. The genotype determines the hereditary characteristics of an individual. A genotype can be determined by sequencing an individual's genome.

GENOTYPING
Genotyping is the process of determining differences in the genetic make-up or genotype of an individual by examining their individual DNA sequence. This can be done by comparing one person's genotype to another individual's sequence, or against a reference sequence.

GLUCAGON
A hormone produced by the pancreas that raises blood glucose levels by promoting the breakdown of glycogen in the liver.

GLYCOGEN
A complex carbohydrate stored in the liver and muscles; serves as a reserve energy source that can be rapidly converted into glucose.

GOLD STANDARD
In medicines development, the gold standard often refers to the best available therapy/product/treatment. Depending on the context, the gold standard may also mean different things. In clinical design, a double-blind, randomized trial is seen by many as the gold standard.
The gold standard may change over time as new methods/treatments/medicines become available. For example, the gold standard test for the diagnosis of aortic dissection (a tear inside the aorta) used to be the aortogram, which had a sensitivity as low as 83% and a specificity as low as 87%. Now, the magnetic resonance angiogram (MRA) is seen by many as the new gold standard test for aortic dissection, with a sensitivity and a specificity both over 90%.

GOOD CLINICAL PRACTICE (GCP)
Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting clinical trials that involve human participants. The International Conference on Harmonization (ICH) has issued a guideline with the objective to provide a unified standard to facilitate the mutual acceptance of clinical data by the regulatory authorities in the jurisdictions pertaining to the ICH.

GOOD DISTRIBUTION PRACTICE (GDP)
Good Distribution Practice (GDP) is a standard ensuring that the quality of a medicine is maintained throughout the distribution network, so that authorized medicines are distributed to retail pharmacists and others selling medicines to the general public without any alteration of their properties.

GOOD LABORATORY PRACTICE (GLP)
Good Laboratory Practice (GLP) is a standard by which laboratory studies are designed, implemented and reported so that there is public assurance that the results are correct and that the experiment can be reproduced exactly at any time in the future.

GOOD MANUFACTURING PRACTICE (GMP)
The purpose of Good Manufacturing Practice (GMP) is to ensure that products are consistently produced according to the appropriate quality standards.
The reliability of the quality of products is guaranteed by controlling the five critical parameters: manpower, environment, equipment, methods, materials.

GOOD PHARMACOVIGILANCE PRACTICES (GVP)
Good Pharmacovigilance Practice (GVP) is a quality standard for monitoring the safety of medicines and if necessary, taking action to reduce the risks and increase the benefits of medicines. It ensures the detection, collection, assessment, understanding, and prevention of adverse effects with medicinal products.

GROUP SEQUENTIAL DESIGN
Group sequential design is an example of a statistical approach in clinical trial design. It means that the sample size of the trial is not fixed in advance, and data is sequentially evaluated as it is collected. This is known as interim analysis, and might be carried out at several points in time. The trial can be stopped when significant results are seen, or if the interim analysis shows that there are safety concerns, or that the trial will

not in fact be able to give a significant result. In this case no more recruitment of patients or further sampling from the patients involved will occur.
Before the trial starts, the 'stopping rule' (i.e. the reason for stopping) must be documented and explained. The stopping rule is a description of exactly what the interim analysis must show to cause the trial to be stopped.
Group sequential analysis can lead to a conclusion much earlier than would be possible with a classical design. It can therefore save time and resources, and reduces the exposure of patients to inferior treatments.

H

HALF LIFE
The time required for half the amount of a medicine to be eliminated from the body.

HAZARD RATIO
A hazard ratio is a measure of how often a particular event happens in a defined period of time in one group compared to how often it happens in another group.

HbA1c
Hemoglobin A1c, a measure of average blood glucose levels over the past two to three months; used as a marker of long-term blood glucose control in diabetes.

HEALTH AUTHORITIES
Government agencies or organizations responsible for overseeing and regulating healthcare policies, practices, and services.

HEALTH TECHNOLOGY ASSESSMENT (HTA)
Health technology assessment aims to inform decision making by health care policy makers. It is a systematic process that considers health technologies (such as medicines) and can involve a review of:

- clinical evidence compared to existing models of care,
- cost effectiveness,
- social and ethical impacts on the health care system and the lives of patients.

The process advises whether or not a health technology should be used, and if so, how it is best used and which patients are most likely to benefit from it. Assessments vary, but most look at the health benefits and risks of using the technology. They can also look at costs and any other wider impacts that the technology may have on a population or on a society. They can also look at the relationship between costs and benefits and risks, and make determinations about value for money.

HEALTH-RELATED QUALITY OF LIFE
Health-Related Quality of Life considers many different aspects related to a person's perception of quality of life affected by health status. These include physical, psychological, functional, and social aspects.

HETEROGENEITY
Clinical diversity (or heterogeneity) is the variability between the patients or the interventions being studied, or between the outcomes that the studies measure. When comparing different studies, it is important to bear in mind that there are several types of heterogeneity.
Methodological diversity (or heterogeneity) refers to variation in study design, and in the risk of bias between studies.
Clinical and/or methodological diversity can lead to differences in the way statistics are applied to different studies (statistical heterogeneity).
Progress in medical science is improving our understanding of heterogeneity among patients with the same disease. The differences in patient responses to treatment, and the risk of adverse reactions, are being explored at the molecular level. This is leading to the development of targeted treatments for different subgroups of patients.

HYPERGLYCEMIA
High blood glucose levels, often associated with diabetes or other metabolic disorders.

HYPOTHESIS
A hypothesis is an assumption, or set of assumptions, made on the basis of limited evidence that either:

- asserts something as a starting point for further investigation or
- confirms something as highly probable in light of established facts.

For a hypothesis to be a scientific hypothesis, it is required that one can test it. A working hypothesis is a provisionally accepted hypothesis proposed for further research.
For the purposes of medicines development, the interest is in the hypothesis that asserts something, for example, that a new treatment for a disease is better than the existing standard of care treatment.

HYPOTHESIS TESTING

Hypothesis testing is the use of statistics to determine the probability that a hypothesis is true. It comprises four steps:

1. Formulate the null hypothesis.
2. Choose the appropriate statistical tests.
3. Perform the test.
4. Accept or reject the null hypothesis.

I

IDENTIFIED RISK
An adverse event for which there is adequate evidence of an association with the use of the medicinal product of interest.

IDIOSYNCRATIC DRUG REACTION
A reaction that occurs rarely and unpredictably in a small percentage of the population in response to a treatment or medicine. These reactions frequently occur with exposure to new medicines and cannot be explained by the known mechanisms of action of the medicine, do not occur at any dose in most patients, and develop mostly unpredictably in susceptible individuals only. Based on the underlying mechanisms, idiosyncratic reactions can be differentiated into (1) immune-mediated hypersensitivity reactions such as skin rashes to serious systemic symptoms (2) reactions involving non-immune individual susceptibility, often related to abnormal production or detoxification of cytotoxic metabolites

IMMUNE ACTIVATION
Stimulation of the immune system in response to a perceived threat or foreign substance.

IMMUNE RESPONSE
The body's coordinated reaction to an invading pathogen or foreign substance, involving various components of the immune system.

IMMUNOGENIC
The ability of a substance to produce an immune response.

IMMUNOTOXICITY
Immunotoxicity is harm occurring to the immune system caused by exposure to chemical substances. Testing for immunotoxicity is a standard part of developing substances as potential new medicines. Symptoms of immunotoxicity can include increased rates or severity of infectious diseases or cancer. Toxic agents can also cause autoimmune diseases, in which healthy tissue is attacked by the body's own immune system. Allergy is another form of immunotoxicity, and many chemicals are known to induce allergic reactions in some people.

IMPARTIAL WITNESS
The role of an impartial witness is to attend the informed consent process if the patient/participant or their legally authorized representative (LAR) cannot read. The impartial witness reads the relevant documentation supplied to the participant (for instance, the consent form). The witness must be independent of the research and may not be unfairly influenced by those involved in the trial. They may, for example, be a non-research member of staff or the patient's relative.

INCIDENCE
The number of new cases of a health event (such as development of a disease, or reaction to a medicine) that occur during a specific time period, usually a year, in a specified population. Incidence is therefore also a measure of the risk of experiencing the health event during a certain period of time.

INCLUSION CRITERIA
Inclusion criteria are the characteristics that potential participants must have in order to be considered for participation in a trial. They describe the patient population and patient selection criteria.
Inclusion criteria should specify the type of testing used to make the patients' diagnosis, as well as specific disease requirements (for example, how severe the disease is, failure or success with previous treatments, plus any other factors that might affect prognosis such as age, sex, or ethnicity).
The inclusion criteria (and exclusion criteria) are important parts of a trial protocol. If they are properly defined, inclusion and exclusion criteria will increase the chances that the trial produces reliable results. They also protect participants from harm and minimize the risks.

INDICATION
In medicine, indication refers to a health condition (therapeutic area) for which a specific intervention (medicinal product, medical device, treatment, procedure) is developed to cure, relieve symptoms, prevent or

diagnose. The indication, as specified in the Summary of Product Characteristics (SmPC) document, determines the boundaries of lawful use of such medicinal product.

INFORMED CONSENT
Informed consent is a person's voluntary agreement, based on an understanding of the relevant information, to participate in research or a clinical trial, or to undergo a particular medical intervention.
Before any research may be carried out, participants must be informed about all aspects of the study and/or intervention, including the aims, methods, anticipated benefits, and potential risks. Participants must also be made aware that they can withdraw from the research at any stage without any negative consequences to their ongoing care or treatment. This information must be given in an accessible and understandable way (for instance via a participant information sheet), and individuals should be given the opportunity to ask questions about the research.
Informed consent is usually documented in writing with a signed and dated consent form. However, informed consent should be an ongoing process throughout a study, and researchers should ensure that participants are made aware of any new information which might influence their decision about whether to take part or not.
In rare circumstances (for example, when an individual may not be able to give informed consent), the usual practices for informed consent may not be possible. Researchers may obtain delayed consent (for instance, for research into emergency situations) or consent by proxy (when the ability to consent is delegated to someone else). In some cases, informed consent may be implied by a person's actions or inaction or silence.

INNOVATIVE CHARACTERISTICS
In medicinal products, this may be defined as offering additional clinical efficacy or effectiveness as compared to the current best standard of care. Improvement to the use of a medicine in addition to an added clinical benefit (such as convenience to patients of, for example, a different mode of delivery, or other characteristics that may improve adherence to therapy, with resulting improvements in clinical outcomes and/or quality of life) may also be considered innovative characteristics.

INSULIN
A hormone produced by the pancreas that regulates blood glucose levels by facilitating the uptake of glucose into cells.

IN-SILICO
Refers to experiments, studies, or analyses conducted using computer simulations or computational models.

INTENTION-TO-TREAT (ITT)
Intention-to-treat (ITT) is an analysis of the participants taking part in a clinical trial, based on the group to which they were initially assigned, and not on the treatment eventually received. It does not matter if they drop out, whether they fully adhere to the treatment, or even if they switch to an alternative treatment. Intention-to-treat analyses are often used to assess the effectiveness of a new treatment because they are seen to reflect real life: not everyone adheres to the treatment they are given, and doctors often change treatments depending on how their patient's condition changes.

INTERIM ANALYSIS
In clinical trials and other scientific studies, an interim analysis is an analysis of the current data from an ongoing trial, in which the primary research question is addressed. It has the potential to modify the conduct of the study. Depending on the results, an interim analysis may lead to changes, such as stopping one treatment arm or changing the number of participants in a group, or stopping the trial altogether.
An example of an interim analysis leading to the early stopping of a study comes from a trial to better identify patients with coronary heart disease who would benefit from an implantable device. The trial compared the devices to treatment with medicines in patients who had survived life-threatening coronary events. The trial was stopped when interim analysis showed a significant reduction in all causes of death in patients assigned to treatment with the implantable device.
An interim analysis requires careful advanced planning and appropriate adjustments to the statistical approach. An interim analysis and any anticipated changes to the trial must be described and justified in the study protocol. The option to modify the design of an ongoing clinical trial is becoming increasingly common and is known as adaptive design.

INTERMEDIATE ENDPOINT
In clinical trials, intermediate endpoints are measures that may be associated with disease status or progression toward a primary endpoint (such as mortality or morbidity). It may be a measure of a body function or disease symptoms (e.g. measures of lung function in chronic obstructive pulmonary disease (COPD)) that is expected to correlate with changes observed on primary endpoints. Clinical trials are often designed to measure changes of an intermediate endpoint and evaluate the effects of an intervention on clinical outcomes.

INTERNAL VALIDITY
Internal validity in a clinical trial is the ability of the trial to reach the correct conclusion about whether or not, and to what extent, a treatment is causing a measured effect on the participants. It implies accurate and unbiased measurement of that effect.
Internal validity is achieved when possible alternative explanations for the measured effect can be excluded, such as chance or bias. Well-designed clinical trials take this into account, for example by using randomization and blinding.

INTERNATIONAL COUNCIL FOR HARMONIZATION (ICH)
Formerly the International Conference on Harmonization. The International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) produces harmonized guidelines for global pharmaceutical development, and their regulation. It brings together the regulatory authorities and the pharmaceutical industry from five regions (Europe, Japan, USA, Canada and Switzerland).
ICH has been established in order to reduce the duplication of clinical trials and create a more streamlined regulatory assessment process for new applications. As such, ICH has developed four sets of guidelines provided for specific topics including quality, safety, efficacy and multidisciplinary (e.g., ICH medical terminology (MedDRA), or the Common Technical Document (CTD)) which are implemented by the regulatory authorities of its membership.

INTERVENTION
In medicine, intervention is an action which changes the outcome or course of a condition or disease so as to prevent harm or improve health through the use of treatments, medicinal products, medical devices or procedures/surgery.

INTERVENTIONAL STUDY
An interventional study is one in which the participants receive some kind of intervention, such as a new medicine, in order to evaluate it. In the medicines development process, medicines are evaluated through interventional studies known as clinical trials.
There are many variations in how clinical trials are designed, but they are commonly randomized (participants are allocated to different arms in the study randomly) and controlled (the study medicine is given to one arm, and the outcomes are compared with an alternative treatment or placebo given to another arm). These are called randomized controlled trials, or RCTs.

INTRAVENOUS
Intravenous means within the vein. It is the infusion of liquid directly into a vein using a syringe or intravenous catheter (tube).
Compared with other routes of administration, the intravenous route is the fastest way to deliver fluids and medicines into the blood stream (the systemic circulation). In intravenous therapy, the bioavailability of the medication is 100%.

INVESTIGATIONAL MEDICINAL PRODUCT (IMP)
An investigational medicinal product (IMP) is an active ingredient or placebo that has been pharmaceutically formulated (prepared) for human use which is being tested, or used as a comparator, in a clinical trial.
Typically IMPs have not yet received marketing authorization, however in some circumstances they may be products that have been authorized:

- when they have been made using a different formulation than that which is authorized (e.g. different dose),
- when the authorized product is to be used as the test substance or comparator in a clinical trial,

- when used for an unapproved indication (off-label), or
- when used to gain further information about an approved use.

INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)
The Investigational Medicinal Product Dossier (IMPD) is an evolving document containing currently available information about an investigational medicinal product (IMP). It includes summaries of information related to the quality, manufacture and control of any IMP (including reference product and/or placebo), data from non-clinical studies and from its clinical use, and the product's phase of development.

INVESTIGATIONAL PLAN
An investigational plan is a medicines development plan to support the authorization of a medicine for humans. It aims to ensure that the necessary data is obtained through clinical and other studies.

INVESTIGATOR
A clinical trial investigator is responsible for the conduct of the trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the leader responsible for the team, and is called the principle investigator.

INVESTIGATOR'S BROCHURE (IB)
The Investigator's Brochure (IB) is a comprehensive document that summarizes all the relevant clinical and non-clinical information about the medicine being studied in humans.
An IB contains a 'Summary of Data and Guidance for the Investigator' section, the aim of which is 'to provide the investigator with a clear understanding of the possible risks and adverse reactions, and of the specific tests, observations, and precautions that may be needed for a clinical trial.'
The IB also provides information to help with the clinical management of participants taking part in the clinical trial.
The sponsor (the organization running and overseeing the trial) is responsible for keeping the information in the IB up-to-date. The IB is of critical importance. It should be reviewed annually and must be updated when any new and important information becomes available, such as when a medicine has received marketing approval and can be prescribed for use commercially.
Owing to the importance of the IB for the safety of participants in clinical trials, the International Conference on Harmonization (ICH) has prepared a detailed guidance document for the authoring of the IB in the European Union, Japan, and the United States.

IN-VITRO
Latin term meaning "within the glass" and referring to experiments or studies conducted outside of a living organism, typically in a controlled laboratory environment.

IN-VIVO
Latin term meaning "within the living" and referring to experiments or studies conducted within a living organism.

L

LEAD
Potential drug candidate or molecule identified as having therapeutic potential during the drug discovery process.

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)
A legally authorized representative (LAR) is an individual authorized (for example by a court) to make decisions on behalf of another person. In circumstances where a patient is unable to give informed consent themselves (for instance, patients in critical care units), sometimes a legally authorized representative can give consent or permission on their behalf, including about medical treatments.

LIFE YEARS GAINED
Life years (LY) gained is a measure in health economics. It expresses the additional number of years of life that a person lives as a result of receiving a treatment.

LIFE-CYCLE MANAGEMENT
Strategies and activities aimed at optimizing the development, marketing, and use of a drug or medical product throughout its life cycle.

LIFETIME PREVALENCE
Lifetime prevalence is the proportion of a population that, at some point in their life, has experienced a particular health event, risk factor or disease. For example, in a survey, you might be asked if you have ever smoked. Lifetime prevalence is calculated by comparing the number of people found to have experienced the health event with the total number of people studied.

LIVER
An organ responsible for various metabolic functions, including glycogen storage, glucose production, and detoxification.

LOG-RANK TEST
A statistical test to compare the survival distributions of two (or more) groups.
This test is used when one wants to test the null hypothesis: that there is no difference in the probability of an event (e.g. death) between the two groups at any time point. The analysis is based on the times of events (or deaths), and it is most likely to detect a difference between the groups compared when the risk of an event is greater for one group.

LOSS TO FOLLOW-UP
Loss to follow-up refers to participants who are no longer actively participating in a study or trial and cannot be contacted for further data collection or follow-up visits. This loss can occur for various reasons, such as participants withdrawing consent, moving away, or becoming unreachable for other reasons. It can lead to missing data and affect the validity and reliability of study results.

LOW-INTERVENTION CLINICAL TRIAL
A low-intervention clinical trial studies an authorized medicine. Its use according to the trial protocol follows the terms of the marketing authorization, or published scientific evidence on safety and efficacy. Any additional procedures must not pose more than minimal additional risk or burden to the safety of the participants compared to normal local clinical practice. Low-intervention clinical trials are used for example to investigate safety and efficacy questions that have arisen since authorization.

M

MARKET EXCLUSIVITY
The 10-year period after the marketing authorization of an orphan medicine, during which similar medicines for the same indication cannot be placed on the market. Market exclusivity should not be confused with market protection or data exclusivity, market exclusivity refers only to orphan medicines.
In this period, the EMA (the European Medicinal Agency) and the member states shall not accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar medicinal product. This protects the original marketing authorization holder from market competition with similar medicines with similar indications once they are approved and is intended to encourage the development of medicines for rare diseases.
The period of market exclusivity is extended by two years for medicines that also have complied with an agreed pediatric investigation plan (PIP).

MARKETING AUTHORIZATION (MA)
Marketing authorization (MA) refers to the approval for a medicine to be marketed.
A system of marketing authorization was put in place to protect public health. Marketing authorizations are granted only when a competent authority (or regulatory authority) has conducted a scientific evaluation, and is satisfied that a medicine is sufficiently safe and effective, and of high enough quality.
Different procedures exist to obtain a MA. The EMA (the European Medicinal Agency) is responsible for the centralized procedure. A single application is submitted to the EMA for evaluation by the Agency's Scientific committees. If the assessment is positive, a single marketing authorization is issued by the European Commission. The Marketing Authorization Holder can then legally begin to market the medicine in all EEA (European Economic Area) countries (EU member states and the three EEA EFTA States (Iceland, Liechtenstein, and Norway).
National Competent Authorities (NCAs) are responsible for evaluation of marketing authorization applications and granting MAs for medicines that fall outside the scope of the centralized procedure. Companies can apply for authorization of these medicines in several countries simultaneously, using the decentralized procedure. Or, once a medicine is authorized in one EU member state, a company can apply for this authorization to be recognized in other EU countries (the mutual recognition procedure). These procedures result in national MAs for each member state involved.

MARKETING AUTHORIZATION HOLDER (MAH)
A Marketing Authorization Holder (MAH) is a company, firm or non-profit organization that has been granted a marketing authorization. The marketing authorization allows the holder to market a specific medicinal product, in one or more EU member states. Once a medicinal product is marketed and in use by patients, the MAH continues to be responsible for monitoring safety (pharmacovigilance). Any suspected adverse reactions must be reported to the body which granted the marketing authorization, in the form of a periodic safety update report (PSUR).

MAXIMUM TOLERATED DOSE (MTD)
The maximum tolerated dose (MTD) is the highest dose of a medicine or treatment that will produce the desired effect without resulting in unacceptable side effects. It is determined in clinical trials by testing increasing doses on different groups of people until the highest dose with acceptable side effects is found. Establishing the maximum tolerated dose is the main objective of Phase I clinical trials.

MEDICAL DEVICE
A medical device is an instrument, apparatus, implant, software or related article used to diagnose, prevent, or treat disease or other conditions. It must not achieve its primary intended action in or on the human body through pharmacological, immunological or metabolic means, but may be assisted in its function by such means.

Medical devices vary greatly in complexity and application. They are intended by the manufacturer to be used for:

- Diagnosis, prevention, monitoring, treatment, or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of, or compensation for an injury or handicap
- Investigation, replacement, or modification of the anatomy or of a physiological process
- Birth control

MEDICAL SUBJECT HEADINGS (MeSH)
Medical Subject Headings (MeSH) is an online controlled vocabulary that lists words, groups of synonyms and related concepts, for the purpose of indexing journal articles and books in the life sciences that facilitates searching.
It was created and updated by the United States National Library of Medicine (NLM), it permits searching at various levels of specificity and allows retrieval of documents in different languages. MeSH is also used by ClinicalTrials.gov registry to classify which diseases are studied by trials registered in ClinicalTrials.gov.

MEDICAL TECHNOLOGY ASSESSMENT
The objective evaluation of a medical technology regarding its safety and performance, its (future) impact on clinical and non-clinical patient outcomes as well as its interactive effects on economical, organizational, social, juridical and ethical aspects of healthcare. Medical technologies are assessed both in absolute terms and in comparison to other (combinations of) medical technologies, procedures, treatments or doing-nothing.

MEDICINES DEVELOPMENT
The term medicines development refers to the scientific and regulatory processes put in place in the attempt to bring a new medicine to the market. It is often used synonymously with drug development. EUPATI and have INNODIA chosen to use the term medicines development throughout their texts.

MEDICINES REGULATION
Medicines regulation is a system that promotes and protects public health. It applies scientific knowledge and is based on national and international laws, to prevent the use of medicines that do not work, are of poor quality, and/or that may be harmful.

Systems vary around the world but generally medicines regulation aims to:

- Assess the safety, efficacy and quality of medicines, and issue marketing authorizations
- License and monitor manufacturers and dispensers of medicines
- Monitor the quality of medicines
- Monitor the safety of medicines under development and in general use including collecting and analyzing adverse reaction reports
- Provide independent information on medicines to professionals and the public

META-ANALYSIS
Meta-analysis refers to methods used to compare and combine results from different, completed (reported or published), independent studies. It aims to identify patterns, to verify results, and to identify relevant relationships arising from multiple studies.
Meta-analysis can be thought of as conducting research about previous research. In its simplest form, meta-analysis is done by identifying a common statistical measure that is shared between studies, and calculating an average of that common measure.
The reason for doing a meta-analysis is to achieve a higher statistical power, as opposed to a less precise measure calculated from a single study. In performing a meta-analysis, an investigator must make many choices which can affect the results. Such choices may include, for example, how to search for studies, how to select or exclude studies, how to deal with incomplete data, and how best to analyze the data.

MICROBIOTA
The community of microorganisms (bacteria, fungi, etc.) that inhabit a particular environment, such as the gut microbiota.

MICROARRAY
DNA microarray analysis is a technique that scientists use to determine whether genes are switched on or off. If a gene is switched on, it is known as gene expression. Scientists use DNA microarrays to measure the

expression levels of thousands of genes at the same time. The result is known as an expression profile. This technique is used in many areas of biological and medical research. It can give valuable information about, for example, what genetic changes are responsible for tumor growth in specific individuals, or whether the expression profile of an individual makes them suitable for a specific treatment.

MICROGRAM
Microgram (µg) is a metric system unit of mass. A µg is equal to one millionth of a gram. Micrograms are typically used in a laboratory setting in early medicines development, or when measuring the concentration of a medicine in the blood.

MINIMAL ANTICIPATED BIOLOGICAL EFFECT LEVEL (MABEL)
The Minimal Anticipated Biological Effect Level (MABEL) is the anticipated dose needed to result in a biological effect in participants of a clinical trial. It is a safety window based on pharmacological threshold. The minimal anticipated biological effect level is recommended as a useful approach to calculate the Safe Starting Dose, as it is the lowest dose that is active.

MISCONDUCT
Scientific misconduct is unethical behavior or the failure to follow established guidelines (such as Good Clinical Practice) in scientific research.
Misconduct includes making things up, changing or lying about research, or copying the work of others (plagiarism). It also includes the failure to follow established guidelines where that failure is deliberate or dangerous researchers have a duty of care to participants in clinical trials and must take reasonable steps to protect their health and data privacy.
Scientists could be found guilty of misconduct in research if they conceal misconduct by others. The MRC's definition does not include honest error or honest differences in designing or carrying out research. Similarly, it does not include poor research unless there is 'intention to deceive'.

MOLECULE
A group of atoms bonded together, representing the smallest fundamental unit of a chemical compound that retains its chemical properties.

MOLECULAR BIOMARKER
A biological marker, or biomarker, is something that can be measured, which points to the presence of a disease, a physiological change, response to a treatment, or a psychological condition.
A molecular biomarker is a molecule that can be used in this way for example, glucose levels are used as a biomarker in managing diabetes. Non-molecular biomarkers include medical images (for example, MRI brain images can provide information about the progression of multiple sclerosis).
Biomarkers are used in many scientific fields. They are used in different ways at different stages of medicines development, including in some cases as a surrogate endpoint to indicate and measure the effect of medicines in trials. For example, hemoglobin levels have been used in Phase III trials to support development of therapies for Type 1 Gaucher disease. This is a rare disease that affects multiple organ systems and shortens life expectancy, but it can take years to show any clinical changes. Therefore, clinical changes are not a good way to evaluate the impact of new treatments for this disease, and biomarkers that show earlier changes are required.

MONOCLONAL
"Monoclonal" refers to a cell population or to a type of antibody derived from a single clone of cells.

MONOCLONAL ANTIBODY
Monoclonal antibodies are created by cloning a unique white blood cell (B cell) or plasma cell to produce identical copies of itself, resulting in a large population of identical antibodies. These antibodies are highly specific and can target a particular antigen. Monoclonal antibodies can be engineered to recognize and bind to specific targets on cells, such as proteins or receptors, to interfere with their function. Monoclonal antibodies have numerous applications in medicine, including diagnostic tests, targeted therapies for autoimmune diseases ad T1D, and as tools for research.

MULTI-ARM MULTI-STAGE (MAMS)
Multi-Arm Multi-Stage (MAMS) trials have a specific design that allows for several different treatments to be evaluated simultaneously against the standard treatment in a single trial.

MULTIPLE ASCENDING DOSE (MAD)
A type of clinical trial where participants receive multiple doses of a drug over a period to assess safety, tolerability, and pharmacokinetics.

MUTUAL RECOGNITION PROCEDURE
The mutual recognition procedure is the system for medicines authorization by individual member states (Concerned Member States) recognizing the authorization of another member state (the Reference Member State) which has evaluated and authorized a new medicine.

N

NATIONAL COMPETENT AUTHORITY
A National Competent Authority or regulatory authority has the power to grant marketing authorizations for medicinal products in its territory.
National competent authorities are organizations that have the legally delegated or invested authority, or power to perform a designated function, normally monitoring compliance with the national statutes and regulations.

NATIONAL PROCEDURE (NP)
Independent national procedures are strictly limited to medicines which are to be authorized and marketed in only one Member State (MS). This procedure is nowadays rarely followed for new products.

NEW DRUG APPLICATION (NDA)
A New Drug Application (NDA) is a document submitted to the Food and Drug Administration (FDA) to request authorization to market a medical product in the United States. The information in the NDA must allow the FDA to make the following judgements (quoted from FDA website):

- Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks
- Whether the drug's proposed labelling (package insert) is appropriate, and what it should contain
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity

The NDA must include information about the medicine's ingredients, outcomes of the animal and clinical studies, how it behaves in the body, and how it is manufactured and packaged.

NEW MOLECULAR ENTITY (NME)
New Molecular Entities (NMEs) are compounds that emerge from the process of medicine discovery, that are not a version or derivative of an existing, previously investigated/approved substance. They have promising activity against a particular target thought to be important in a disease, however, little is known about the efficacy, safety, toxicity, pharmacokinetics and metabolism in humans. A full development program of non-clinical and clinical trials must be performed to evaluate the potential of an NME to become a medicinal product.

NO OBSERVED ADVERSE EFFECT LEVEL (NOAEL)
The no observed adverse effect level (NOAEL) is the highest tested dose of a medicine at which there is no increase in the frequency of any adverse effects (biological or statistically significant) when compared to its control.
Although the NOAEL approach involves some consideration of pharmacokinetics and pharmacodynamics properties, its focus is on the estimation of the highest safe dose, looking for a safety window based on toxicological threshold.

NON-CLINICAL TESTING
Non-clinical testing is conducted at a stage of medicines development that uses animals and/or cells or tissues. It does not involve testing in humans. The main goal of non-clinical tests is to determine the safety of a medicine. Non-clinical testing will investigate any harmful effects of the medicine on the body due to the medicine's pharmacology, such as:

- Toxic effects - for example, on the reproductive system
- If the medicine causes genetic changes
- For some substances, whether they might cause cancerous growth.

Toxicity will be measured in relation to different doses, or length of use of the medicine. The reversibility of any toxicity will also be studied.
Information from non-clinical testing is used in planning clinical trials in humans. It is used to decide what the

starting dose should be, and the range of does to be tested. It also suggests what clinical signs should be looked for in order to detect any adverse effects.

NON-INTERVENTIONAL OBSERVATIONAL STUDY

In epidemiology and statistics, an observational study draws conclusions about the possible effect of a treatment on participants, where the assignment of participants into a treatment group versus a control group is outside the control of the investigator. In a non-interventional observational study, no additional diagnostic or monitoring procedures are applied to the patients, and epidemiological methods are used for the analysis of collected data (as per Article 2(c) of 2001/20/EC). It is not a randomized, controlled trial (RCT).
However, in some cases, observational studies are the most appropriate design, for example, if the condition being studied is rare. Sometimes non-interventional studies are the only ethical approach, for example if the effect of an environmental risk factor such as asbestos is being studied, it would be unethical to deliberately expose participants to asbestos.
There are three types of non-interventional study, which are defined separately in this glossary. They are:

- Cohort studies
- Cross-sectional studies
- Case-control studies

NON-RANDOMIZED TRIAL

In a non-randomized clinical trial, participants are allocated to different treatment (or placebo) arms using a non-random method. Allocation is decided and managed by the investigator. Non-random allocation can lead to bias in the results of a trial.

In the description above, the non-randomized trial is controlled (arms receiving an intervention are compared with arms that are receiving different interventions or placebo). There are several other trial designs that are non-random, but controlled. These include prospective observational studies.

NULL HYPOTHESIS

The word “null” can be thought of as “no change”. A null hypothesis is typically the standard assumption and is defined as the prediction that there is no interaction between variables.

For example, the null hypothesis states that there is no causal relationship between a new treatment and a reduction in disease symptoms. In other words, this means that a new treatment does not offer an improvement over the standard of care treatment and that any observations of improvement are the result of chance.
Such a statement can be tested by a scientific study such as a clinical trial and the application of appropriate statistical tests. If a clinical trial finds that in fact there is a relationship, and the new treatment causes an improvement, the null hypothesis is disproved and can be rejected. In this case the alternative or research hypothesis can be adopted in this example, this means that the new treatment is better than the standard of care treatment.

NUMBER-NEEDED-TO-TREAT (NNT)

The number-needed-to-treat (NNT) is a measure used to describe the effectiveness of an intervention, such as treatment with a medicine.
The NNT is the number of participants who will need to be treated in order for one person to recover, or show symptom reduction, or whatever outcome is being measured in the trial. A “perfect” result would be that every patient has a good outcome, and this would give an NNT of 1. A large NNT means that the treatment is only effective in a small number of people: An NNT of 100 means that of 100 people treated, only 1 will have a favorable outcome.
One advantage of NNTs is that they can be easily compared for different medicines or interventions.

O

OBSERVATIONAL STUDY
In epidemiology and statistics, an observational study draws conclusions about the possible effect of a treatment on participants, where the assignment of participants into a treatment group versus a control group is outside the control of the investigator.
However, in some cases observational studies are the most appropriate design for example if the condition being studied is rare. Additionally, non-interventional observational studies are sometimes the only ethical approach. For example, if the effect of an environmental risk factor (such as asbestos) is being studied, it is unethical to deliberately expose participants to that risk factor.
In a non-interventional observational study, no additional diagnostic or monitoring procedures are applied to the participants, and epidemiological methods are used for the analysis of collected data (as per Article 2(c) of 2001/20/EC). A non-interventional observational study is not a randomized, controlled trial (RCT).

OBSERVER BIAS
Observer bias (also called ascertainment or detection bias) is caused when the actions of an investigator affect the results of a trial. Observer bias can be unintentional and could arise from the investigator's hopes or expectations of the trial. It is most likely to occur when:

- the investigator's personal judgement is used to measure subjective trial outcomes, and
- the investigator knows which group each person is allocated to (for example treatment or placebo).

The most important design technique for avoiding observer bias in clinical trials is blinding. The potential effect of bias should also be taken into account during statistical analysis of trial data.

OBSERVER-REPORTED OUTCOME
A measurement based on an observation by someone other than the patient or a health professional such as a parent, or other non-clinical caregiver who regularly observes the patient in daily life and is in a position to report on a specific aspect of the patient's health.
This type of measure or observer report is without medical judgment or interpretation, and includes events or behaviors that can be observed in patients who cannot communicate themselves (e.g. infants or cognitively impaired).

OFF-LABEL USE
Off-label use refers to situations where a medicinal product is intentionally used for a medical purpose other than what is stated in the authorised product information, i.e. the Summary of Product Characteristics (SmPC). Examples of off-label use include non-authorized:

- indication
- age group
- dosage
- route of administration

OFFICIAL MEDICINES CONTROL LABORATORY (OMCL)
An Official Medicines Control Laboratory (OMCL) is a public institution which performs laboratory testing on medicines once they are on the market. They are an essential part of the European system of controlling the quality of medicines.
OMCLs are appointed by national competent authorities. OMCLs carry out testing for their competent authority, independently from the manufacturer of the medicine. OMCLs in Europe collaborate with each other in order to pool resources and share best practice.

OMICS TECHNOLOGIES
The Omics technologies are relatively recent fields of study such as genomics, proteomics, or metabolomics. They deal with large amounts of data because they assess entire genomes, proteomes, or metabolomes. Information technology (IT) is therefore a crucial element in omics research.

ONCOGENE
An oncogene is a mutated gene that contributes to the development of a cancer. In their normal, non-mutated state, oncogenes are called proto-oncogenes, and they are important in the regulation of cell growth. When altered, an oncogene can either promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by exposure to carcinogens (cancer-causing substances).

OPEN-LABEL TRIAL
A clinical trial where both the researchers and participants know which treatment is being administered, as opposed to a blinded trial.

ORAL GLUCOSE TOLERANCE TEST (OGTT)
A diagnostic test used to assess how the body metabolizes glucose over time, typically involving the ingestion of a glucose solution followed by blood glucose measurements at regular intervals. Fasting blood is drawn to determine baseline glucose level followed by ingestion of 75 g of glucose dissolved in 250-300 ml of water. Blood is drawn again after two hours and glucose level determined. Plasma glucose over 200 mg/dL (11.1 mmol/L) confirms a diagnosis of diabetes.

ORPHAN DESIGNATION
Orphan designation is a special status for a medicine used to treat a rare disease or condition. An orphan designation is adopted by the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) and confirmed by the European Commission (EC) before the granting of marketing authorisation.
To qualify for orphan designation, a medicine must meet a number of criteria:

(1) It must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating
(2) The condition must affect no more than 5 in 10,000 people in the EU, or it must be unlikely that sales of the medicine will be sufficient to justify the investment needed for its development
(3) No satisfactory method of diagnosis, prevention or treatment of the condition exists, or, if it does, the medicine in question must provide a significant benefit to those affected by the condition

Developers of medicines who obtain orphan designation benefit from a number of incentives. Incentives include specific scientific advice and 10-year market exclusivity. Market exclusivity means that, during this period, no other medicine for the same condition will be granted market authorisation. Reduced fees for applications for services from the European Medicines Agency (EMA) may also be available.

ORPHAN MEDICINE
An orphan medicine is a medicine that has been developed specifically to treat a rare condition (an orphan disease). Orphan medicines generally follow the same regulatory development path as any other medicine, however, some incentives are provided to encourage a manufacturer to invest in developing them. An orphan designation is adopted by the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) and confirmed by the European Commission (EC) before the granting of marketing authorization.
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The incentives for developing orphan medicines include specific scientific advice, and 10 year market exclusivity. Market exclusivity means that no other medicine for the same condition will be granted market authorisation during this period. Reduced fees for applications for services from the EMA may also be available.

OVER EXPRESSION

Over expression is when a gene is too active and produces too much of the protein it encodes. Normally a variety of molecular mechanisms ensures that genes are expressed at the appropriate levels at the right times. Many cancers arise through the over expression of key regulatory genes.

P

P-VALUE
A p-value, which stands for probability value, is a statistical measure between 0 and 1. It is used for hypothesis testing. In clinical trials it is used to give an indication of whether a result observed may be due to chance, or not.
A significance level should be set before data collection begins, and is usually set to 5% (or 0.05), although other levels may be used depending on the study.
A result is then said to be statistically significant (and allows us to reject the null hypothesis) if it has a p-value equal to or less than the significance level. This is generally written as $p \leq 0.05$.
In calculating the p-value, we first assume that there really is no true difference between the two tested treatments, e.g. new versus standard treatment (the null hypothesis). We then calculate the likelihood (probability) that the difference we have observed is just due to chance if our supposition is true (that is, if there is really no true difference). This is the p-value.
So, the p-value is the probability to observe effects as big as those seen in the study if there was really no difference between the treatments. If p is small, the findings are unlikely to have arisen by chance and we reject the idea that there is no difference between the two treatments (we reject the null hypothesis). If p is large, the observed difference is plausibly a chance finding and we do not reject the idea that there is no difference between the treatments.

PACKAGE INSERT
The Package Insert (formerly prescribing information) in the United States (USPI), is a document included inside the external packaging of a prescription or over-the-counter medicine to provide information for patients. In Europe, the patient information in the pack is the Package Leaflet (PL) (formerly called the Patient Information Leaflet (PIL)).
The document is subject to detailed regulatory specifications, including approved chemical and proprietary names, descriptions, and classifications clinical pharmacology.

PACKAGE LEAFLET
In the EU, medicinal products must be accompanied by outer and/or immediate packaging information (labelling) and a Package Leaflet (PL). The PL should be written in language understandable by the patient and must undergo readability testing. It contains:

- What medicine X is and what it is used for (identification of the medicinal product)
- What you need to know before you take/use X (contraindications and warnings and precautions for use: in children and adolescents with other medicines

PEDIATRIC INVESTIGATION PLAN (PIP)
A pediatric investigation plan (PIP) is a medicines development plan to support the authorization of a medicine for children. It aims to ensure that the necessary data is obtained through studies in children, when it is safe to do so.
Pharmaceutical companies submit proposals for PIPs to the European Medicine Agency's (EMA) Paediatric Committee (PDCO). This Committee is responsible for agreeing to or refusing the plan.
The normal development of a medicine requires that various studies be performed to ensure its quality, safety, and efficacy. In addition to this, PIPs:

- include a description of the studies and of the measures to adapt the medicine's formulation to make its use more acceptable in children, such as the use of a liquid formulation rather than large tablets
- cover the needs of all age groups of children, from birth to adolescence

PARALLEL-GROUP
A study design where participants are divided into separate groups, with each group receiving a different treatment or intervention simultaneously.

PARENTERAL
Medicines administered via any route other than the gastrointestinal tract (oesophagus, stomach, and small and large intestines). The most frequent are subcutaneous, intravenous and intramuscular injections, but medicines that are topically administered to the eye, ear, and skin or even inhaled may be broadly considered as parenteral.

PASSIVE SURVEILLANCE
Passive surveillance is the use of local healthcare services to collect data on disease incidence or adverse effects of medicines. It relies on staff and services, who are part of a reporting network, collecting data and generating reports. There is no active search for cases.
For example, passive surveillance is the most common method used to monitor the incidence of vaccine-preventable diseases so that national and international bodies can identify possible outbreaks and organise vaccine provisions.

PATENT
A medicine patent is a legal protection granted by a government authority that gives the patent holder exclusive rights to manufacture, use, and sell a specific medicine for a certain period of time. This exclusivity typically lasts for 20 years from the date of filing the patent application. During this time, other manufacturers are prohibited from producing and selling generic versions of the patented medicine. Medicine patents are intended to incentivize innovation and investment in pharmaceutical research and development by providing a period of market exclusivity for new drugs.

PATHOGEN
A bacterium, virus, or other micro-organism that can cause disease.

PATIENT REGISTRY
A patient registry is a collection of information about individuals, usually those with a specific diagnosis or with specific risk factors for a disease. Some patient registries seek people with varying health levels who may be willing to take part in research about a particular disease. Registries can be funded and/or managed by government agencies, non-profit organisations, clinics, or commercial organisations.
Patient registries have multiple uses. For example, registries for rare diseases can be used to establish the basic characteristics of the disease, how it is managed in clinics, and what outcomes people experience. Other uses include helping to measure clinical effectiveness of treatments in 'real world' settings, and investigating quality of patient care.
Clinical trial registries collect basic health information from people who agree to be contacted about taking part in future clinical trials. Volunteering for a registry does not mean a person has signed up for a clinical trial. Volunteering for a disease registry can sometimes become a first step toward taking part in a clinical trial, but registries and specific trials are not directly linked.

PATIENT SELECTION
Patient selection can refer to how patients are matched with proposed treatments (in the clinic), or how patients are selected to take part in clinical trials.
For clinical trials, detailed inclusion and exclusion criteria are documented before recruitment of patients can begin. The inclusion and exclusion criteria are an important part of a trial protocol. If they are properly defined, inclusion and exclusion criteria will increase the chances of a trial producing reliable results. They also protect participants from harm and help avoid exploitation of vulnerable people (such as those without the ability to provide informed consent).

PATIENT-REPORTED OUTCOME (PRO)
A patient-reported outcome (PRO) is a measure of the experience or view of a participant in a clinical study. It is not a clinical measure, or an assessment made by anyone else involved in the study. PROs are commonly collected by asking patients to fill in questionnaires, or by interviewing patients. Questionnaires or interview guides used as part of clinical studies should undergo extensive testing to ensure they are reliable and valid. PROs can be used to assess, for example, symptoms as experienced by the patient, disability, quality of life, and other health perceptions.
There are many published PRO questionnaires dealing with aspects of quality of life. some have been developed for specific conditions or treatments. Some are designed to be general, such as the 'EuroQoL' or

'EQ-5D', which has been translated into many languages and used extensively in clinical trials.
PRO is often used interchangeably with the term patient-reported outcome measure (PROM).

PATIENT-REPORTED OUTCOME MEASURES (PROM)
Patient-reported outcome measures (PROMs) are the tools used to measure and collect data on patient-reported outcomes (PRO). Generally, findings are measured by a well-defined and reliable patient-reported outcome instrument. The use of a PRO instrument is advised when measuring an aspect of the disease or condition that is best known by the patient or is best measured from the patient perspective.

PER PROTOCOL ANALYSIS
An analysis that is restricted to the participants who fulfil the protocol in terms of the eligibility, interventions, and outcome assessment. This analysis restricts the comparison of the treatments outcomes to the participants who adhered perfectly to the clinical trial instructions as stipulated in the protocol, i.e. completed the full treatment. If done alone, this analysis leads to bias because it does not consider participants who did not follow the protocol completely for any reason.

PERIOD OF EXCLUSIVITY
A period of exclusivity refers to a time after a medicine is authorised during which no other similar medicines with the same indications (intended uses) may be authorised. This protects the medicine from competition during the period of exclusivity. There can be several separate market exclusivities relating to designated conditions.
The period of market exclusivity is extended by two years for medicines that have also complied with an agreed paediatric investigation plan (PIP).

PERIODIC SAFETY UPDATE REPORT (PSUR)
A Periodic Safety Update Report (PSUR) is EU terminology for a Periodic Benefit Risk Evaluation Report (PBRER). It is produced by the marketing authorisation holder (the individual or business that is granted authorisation to market a medicine) at defined time points after a medicine has been given marketing authorisation.
The purpose of the report is to provide comprehensive and up to date information about the safety of a medicine. The report should summarise any new evidence on safety, efficacy and effectiveness that might affect the balance of risks and benefits. The PSUR communicates about risk to regulatory authorities and identifies where risk management initiatives may be required.

PERSONALISED MEDICINE
Personalised medicine is a medical model that proposes to customise medical decisions, practices, and treatments for the individual patient. It uses targeted medicines aimed at specific molecules that are involved in the patient's disease and takes genetic, clinical, environmental, and lifestyle information about the patient into account. The aim is to select the best therapies for the individual patient to ensure the best outcome and reduce the risk of side effects.
Progress in understanding the link between genomics (and other molecular factors) and disease is an important part of the development of personalised medicine. Pharmaceutical companies are already producing some targeted medicines as a result.

PHARMACEUTICAL FORM
Pharmaceutical form is the physical characteristics of the combination of active substance and excipients (non-active ingredients) forming a medicinal product (tablet, liquid, capsule, gel, cream, sprays, etc.).

PHARMACODYNAMICS
Pharmacodynamics is the branch of pharmacology that studies what the medicine does to the body. Pharmacodynamics looks at the biological and physiological effects of a medicine, and their mechanisms of action at organ and cellular level.

PHARMACOEPIDEMIOLOGY
Pharmacoepidemiology is the study of the uses and effects of medicines in large numbers of people. It provides an estimate of the probability of beneficial effects of a medicine in a population and the probability of adverse effects. It involves continual monitoring of a population for unwanted effects and other safety concerns.

PHARMACOGENETICS
Pharmacogenetics is the study of individual genetic differences to understand how genes affect a person's response to medicines. Understanding how different genetics affect how a medicine is processed can help doctors to determine which medicine and which dose more accurately is best for each patient according to their response. Pharmacogenetics also helps doctors identify the medicine that best treats a disease and is least likely to cause side effects.

PHARMACOGENOMICS
Pharmacogenomics is the study of entire genomes, across groups of individuals, to identify the genetic factors that influence responses to a medicine. Pharmacogenomics combines traditional pharmaceutical sciences, such as biochemistry, with an understanding of common DNA variations in the human genome.

PHARMACOKINETIC STUDY
A pharmacokinetic study is a study of how a medicine is handled by the body, usually measuring the concentration of the medicine in blood, urine, or tissues over time. Pharmacokinetic studies are used to characterise the absorption, distribution, metabolism, and excretion (ADME) of a compound, either in blood or in other locations, and are often employed at the discovery or candidate-selection stages of a medicine development program.

PHARMACOKINETICS
Pharmacokinetics is the study of what the body does to medicine. It studies the absorption, distribution, metabolism, and excretion of the medicine (ADME), as well as bioavailability.
These pharmacokinetic processes, often referred to as ADME, determine concentration of the medicine in the body, and the onset, duration, and intensity of a medicine's effect.

PHARMACOLOGIST
A pharmacologist investigates how medicines interact with biological systems, using in vitro (cells or animal tissues) or in vivo (live animals) research to predict what effect the medicine might have in humans. Pharmacologists aim to understand how medicines work and if they can be used effectively and safely in humans. They work closely with researchers to aid medicine discovery and development, and to determine questions of causation involving medications.

PHARMACOLOGY
Pharmacology is the study of medicines, including their characteristics, interactions, and uses, and the biochemical or physiological effect they have on the cell, tissue, organ, or organism.

PHARMACOPOEIA
A pharmacopoeia is a collection of official standards for pharmaceutical substances and medicinal products. It includes directions for the quality control tests to be carried out on medicines and the raw materials used in production. It is a vital reference for individuals and organisations involved in research, development, manufacture, and quality control of medicines.
In most countries there is an official pharmacopoeia and all producers of medicines and/or substances for pharmaceutical use must comply with its quality/safety standards. In Europe, the European Pharmacopoeia provides the legal and scientific basis for quality control during development, production and marketing of medicines in European member states.

PHARMACOTHERAPY
Pharmacotherapy is the treatment of diseases using conventional medicines (not biologic medicines).

PHARMACOVIGILANCE
Pharmacovigilance is the practice of detecting, assessing, understanding and preventing the adverse effects of medicines. Pharmacovigilance enhances patient safety and public health by providing reliable information on the risks and benefits of medicines.

PHARMACOVIGILANCE AND RISK ASSESSMENT COMMITTEE (PRAC)
The Pharmacovigilance Risk Assessment Committee (PRAC) is the European Medicines Agency's (EMA) committee responsible for assessing and monitoring the safety of human medicines. The Committee meets once

a month. EMA publishes the agendas, minutes and highlights of its plenary meetings.
https://www.ema.europa.eu/en/committees/pharmacovigilance-risk-assessment-committee-prac

PHASE 0 TRIALS
Phase 0 trials are conducted with sub-therapeutic doses to see if a medicine behaves in the body in the way that earlier laboratory studies (non-clinical trials) predicted.

PHASE I TRIALS
Normally, the first studies in humans with a new medicine are Phase I trials.
Phase I trials are usually conducted in a small number of healthy volunteers (although some trials recruit patients). The aim of Phase I trials is to find out the safe dose range, and to look for any side effects. The initial dose given will be very small, and gradually increased if no or only mild side effects are observed. A new medicine has to meet certain pre-set requirements before it can continue to Phase II trials. Phase I, II, and III trials are commonly known together as 'clinical development'.

PHASE II TRIALS
Phase II trials are generally the first studies with a new medicine in patients. They are usually conducted in a small number of patients who are monitored closely. These trials are often larger than Phase I trials.
Phase II studies are designed to find out if the medicine has a beneficial effect on the disease in question: They might compare the new medicine to an existing treatment or to a placebo. They also set out to determine the best dose range and how often the medicine should be given, and investigate the best way to manage any side effects.
A new medicine has to meet certain pre-set requirements before it can continue to Phase III trials. Phase I, II, and III trials are commonly known as 'clinical development'.

PHASE III TRIALS
Phase III trials are generally large (comprising thousands of patients) and involve several study sites, sometimes in different countries. They compare the new medicine to existing treatments or a placebo, in order to show the safety and efficacy of the new medicine. Most Phase III trials are randomised.
Phase I, II, and III trials are commonly known as 'clinical development'. Phase III studies are critical to applications for marketing authorisation.

PHASE IV TRIALS
Phase IV trials are usually conducted after marketing authorisation is granted and the medicine is in general use.
Phase IV studies are also known as post-authorisation safety studies (PASS) and may be voluntary or imposed by the regulatory authorities. The possibility also exists of requesting the marketing authorisation holder to conduct post-authorisation efficacy studies (PAESs) in order to complement efficacy data that are available at the time of the initial authorisation. Phase IV studies collect additional information about side-effects and safety, long-term risks and benefits, and/or how well the medicine works when used widely.

PIVOTAL STUDY
A pivotal study is normally a Phase III study of a new intervention which is designed to provide the necessary data for a decision by a regulatory agency.
For example, the European Medicines Agency (EMA) requires specific safety and efficacy information about new medicines before it can issue a marketing authorisation. A pivotal study will be conducted to Good Clinical Practice standards. It will generally be randomised and controlled (an RCT). It will be of adequate size and, whenever possible, double-blind.

PLACEBO
In clinical trials, a placebo is a medicine that contains no active ingredients. Placebos have no known medical effects.
The 'placebo effect' is a benefit or side effect perceived by patients taking a placebo, despite the fact that no medicine is involved.

PLACEBO-CONTROLLED
A placebo-controlled trial is one in which a new medicine is tested against a placebo - a medicine that contains no active ingredients.

In placebo-controlled trials, people are assigned to a group (treatment arm) that receives the medicine, or a group that receives the placebo. This is one way to improve the chances that any benefit experienced by the treatment group receiving the medicine is due to the active ingredient in that medicine rather than some other factor.

PLASMA
Plasma is the fluid part of blood. It contains cells, gases, proteins, enzymes, etc. Unlike blood, plasma is yellow.

POPULATION
A population is a group of people who share a common trait. For example, they might have a certain disease of interest to researchers, have the same educational background or type of job, or they might live in a particular region.

POPULATION PHARMACOKINETICS
Population pharmacokinetics is the study of variability in the Absorption, Distribution, Metabolism, and Excretion (ADME) of a medicine between individuals (healthy volunteers or patients). In order to understand how individuals from a population differ from one another, it is necessary to perform population pharmacokinetic analysis.

POSOLOGY
The branch of pharmacology and therapeutics concerned with dosage.

POST AUTHORISATION SAFETY STUDY
A post authorisation safety study is a study carried out after a medicine has been given a marketing authorisation. Its purpose is to obtain further safety information or to assess how well risk-management measures are working. The information from a post authorisation safety study is used in regulatory decision making.

A post authorisation safety study might be a clinical trial or a non-interventional study, and can be created voluntarily by the MAH, or can be required by the regulator (imposed). The Pharmacovigilance Risk Assessment Committee (PRAC) at the European Medicines Agency (EMA) is responsible for assessing the protocols of imposed studies and for assessing the studies' results. The EMA publishes the protocols and abstracts of the final study reports online.

POST MARKETING
Post marketing refers to the period after a medicine has been granted marketing authorisation and is available for general use.

POST-AUTHORISATION EFFICACY STUDY (PAES)
A post-authorisation efficacy study (PAES) may be voluntary or imposed by regulatory authorities. Post-authorisation efficacy studies take place after marketing authorisation is granted and the medicine is in general use. They are Phase IV studies, intended to complement efficacy data that are available at the time of the initial authorisation, and gather long-term data about how well the medicine works when used widely.

POST-MARKETING SURVEILLANCE STUDY (PMS)
A post-marketing surveillance (PMS) study, also known as a Phase IV study, may be voluntary or imposed by the regulatory authorities. They are conducted after marketing authorisation is granted and the medicine is in general use. Post-marketing surveillance studies collect additional information about side-effects and safety, long-term risks and benefits, and/or how well the medicine works when it is used widely.

POTENTIAL RISK
An unexpected event for which there is suspicion of an association with a medicinal product, but where this association has not been confirmed. Some examples are:

- toxicological findings seen in non-clinical safety studies which have not been observed in clinical studies

- adverse events observed in clinical trials or epidemiological studies for which the difference compared with the control group raises a suspicion of an association, but is not large enough to suggest a causal relationship

POWER
A term often used in clinical research is statistical power. The power of a statistical test is the ability of the test to detect an effect, if the effect actually exists. In statistical terms, it is the probability that it will correctly lead to the rejection of a null hypothesis.
In some cases we may not be able to reject the null hypothesis, not because it is true, but because we do not have sufficient evidence against it. This might be because the experiment is not large enough to reject the null hypothesis. As such, the power of a test can be described as the probability of not making a Type II error (not rejecting the null hypothesis when in fact it is false).

PRECURSOR
A substance or cellular component from which another substance or cellular component is formed.

PRE-DIABETES
The Natural History studies of Type 1 Diabetes showed that the biological process leading to the disease onset, often starts months or even years before the symptoms appear and before the disease is diagnosed. During this period, the autoimmune process which will lead to the loss of ß- cell function, has already been triggered. The body starts to produce autoantibodies against ß- cell, while the blood sugar lever are still normal and there are no symptoms of the disease. This phase is also Known as STAGE 1 of Type 1 Diabetes.

PREDICTIVE MEDICINE
Predictive medicine is a field of medicine that predicts the probability of disease. When an individual is predicted to have a high risk of a disease, preventive measures can be started in order to either prevent the disease altogether or significantly decrease its impact upon the patient. Preventive measures might be lifestyle modifications and/or increased monitoring by healthcare professionals.
Predictive medicine changes medicine from being reactive to being proactive, and has the potential to extend healthy lifetimes and to prevent disease. As yet it is not possible to predict with 100% certainty that a specific disease will occur. Predictive genetic testing is one of the key approaches in predictive medicine.

PREDISPOSED
Someone who is predisposed to a disease is more likely than other people to develop the disease in the future.
For example, someone who is genetically predisposed to develop Alzheimer's has a genetic makeup that increases their risk of developing this disease. A predisposition will not in itself cause the disease, but the disease may eventually be triggered by particular environmental or lifestyle factors, such as tobacco smoking or diet. Genetic testing is able to identify individuals who are genetically predisposed to certain diseases.

PRESYMPTOMATIC
Referring to the period before symptoms of a disease appear.

PREVALENCE
Prevalence is the proportion of a population found to have a condition (typically a disease or a risk factor such as smoking). It is calculated by comparing the number of people found to have the condition with the total number of people studied, and is usually expressed as a fraction (for example, 1/3), as a percentage (%) or as the number of cases per 10,000 or 100,000 people.
Prevalence can be measured at a particular point in time (point prevalence), or over a specified period such as a year (period prevalence).

PROBABILITY
Probability is the measure of the likelihood that a particular event will occur.
Probability is quantified as a number between 0 and 1 (where 0 indicates impossibility and 1 indicates certainty). The higher the probability of an event, the more certain we are that the event will occur. A simple example is the toss of a fair (unbiased) coin. Since the two outcomes are equally probable, the probability of 'heads' is equal to the probability of 'tails'. Therefore, the probability of either 'heads' or 'tails' is 1/2 (or 50%).

PROOF OF CONCEPT (POC)
A proof of concept (POC) trial is one type of trial carried out early in the clinical development phase of a medicine (in humans). Phase II trials usually begin with a proof of concept trial, which aims to show that the medicine interacts with its intended target and affects the disease in question.

PROOF OF MECHANISM (POM)
A proof of mechanism (POM) study is normally done within Phase I Clinical Development in healthy volunteers. Such studies are designed to show that a new medicine reaches its target organ(s), interacts with its molecular target, and affects the biology of the target cells as intended.

PROPORTION
A part, share, or number considered in comparative relation to a whole, expressed as a fraction (ratio) or percentage. For example, in epidemiology, the number of people who have a disease compared with the total number of people studied.

PROSPECTIVE COHORT STUDY
In a prospective cohort study, groups of people are identified before they show any signs of disease and are followed up over time. Alternatively, in retrospective cohort studies, data is used that has already been collected (possibly over a long period of time) for other purposes.
Cohort studies are one type of observational study, in which the researcher does not perform any intervention (such as administering a medicine).
Cohort studies are useful when it would be unethical to carry out a randomised controlled trial (RCT). For example, it would be unethical to deliberately expose people to cigarette smoke or asbestos.

PROSPECTIVE META-ANALYSIS
A prospective meta-analysis uses only trials that have been identified and selected before their results are known. This avoids some of the problems of meta-analyses.
Usually, meta-analyses are performed when individual trials have finished. However, collecting studies after their completion can lead to statistical problems. For example, if a meta-analysis is carried out because of knowledge of a particular positive trial result, this can influence how other studies are chosen for the meta-analysis and cause bias in the analysis. This is why prospective meta-analyses are performed.

PROTEOME
The word 'proteome' is derived from 'Proteins expressed by a genome'. It refers to the entire set of proteins expressed and modified by a specific cell, tissue, or organism at a certain time, under defined conditions. The proteome changes constantly in response to intra- and extracellular environmental signals health or disease

PROTEOMIC MARKER
A proteomic marker is one type of biological marker, or biomarker. The term is often used interchangeably with protein marker and is a protein, or set of proteins, used as a biomarker.

PROTEOMICS
Proteomics is a branch of biotechnology that applies the techniques of molecular biology, biochemistry, and genetics to study proteins, how they are modified, their structure, function, and interactions with one another. The goal of proteomics is to obtain a more global and integrated view of biology by studying all the proteins of a cell or tissue rather than each protein individually. Study methods include looking at protein-protein interaction, protein modifications, protein function, and protein localisation.

PROTOCOL
The protocol of a clinical trial is a document that contains:

- The objectives (aims) of the trial
- The trial design, including:
- How participants will be selected
- How many participants are needed;
- What measurements and endpoints will be used; and
- How bias will be minimised

Q

QUALITATIVE STUDY
Qualitative studies are based on collecting information that describes people's perspectives and motivations. Unlike quantitative studies, they do not try to quantify anything or use statistics.
A qualitative study might use focus groups, or interviews or observation, or a combination of methods. Sample sizes (the number of people recruited to take part) are more difficult to predict, and are often smaller than in quantitative studies. Qualitative researchers will often analyse their data as they go along, and stop looking for new people to take part when no new insights are being found.
Qualitative researchers do not assume that they know what the important issues are. Often it is not until the research is underway that the real issues are identified. Therefore, qualitative methods are general designed to give participants the freedom to raise issues that are important to them. For example, topic guides will be developed for interviews rather than tightly defined questionnaires.
Qualitative methods are often used in combination with other methods to provide rich and comprehensive data sets.

QUALITY CONTROL (QC)
Quality Control (QC) is part of the system of ensuring high standards during research, trials and production for medicines. Each step of medicines development and production is managed under a Quality Management (QM) system.
The standards required are known as the Quality Assurance (QA) system, whereas QC is the method used to ensure the standards are met at each step.
Quality management for clinical research is known as Good Clinical Practice (GCP).

QUALITY OF LIFE (QoL)
Quality of Life (QoL) is a measure in health economics. It expresses the effect of factors such as symptoms, pain, psychological health, and wellbeing on people's lives. Health-related quality of life (HRQoL) measures are used to calculate the likely impact of treatments on the lives of patients.

QUALITY-ADJUSTED LIFE YEAR (QALY)
The quality-adjusted life year (QALY) is a measure in health economics. It expresses the additional number of years which a person lives as a result of receiving a treatment, and takes into account the quality of life of those years. It does this by measuring how important various factors are to patients, such as symptoms, pain, and psychological health.
The calculation of QALYs is a common approach used by health technology assessment (HTA) bodies, which advise about the 'usefulness' of treatments and, in some countries, about whether treatments should be funded by (for example) government health departments.

QUANTITATIVE STUDY
A quantitative study aims to measure and quantify, and uses statistical methods to analyse data. Unlike qualitative studies, they do not collect information about people's perspectives and motivations.

QUASI-RANDOMISED TRIAL
A quasi-randomised trial is one in which participants are allocated to different arms of the trial (to receive the study medicine, or placebo, for example) using a method of allocation that is not truly random.
Allocation might be based on date of birth, medical record number, or the order in which people were recruited (for example, every other person might be allocated to the placebo group).
With quasi-randomisation there is a greater risk that the investigator will be aware of which participant is in which group. There is therefore a risk of selection bias.

R

RANDOMIZATION

Randomization is a method of allocating or selecting without using any system. It is purely random. In clinical trials, participants are generally allocated to different arms of the trial (for example, to receive the study medicine or the placebo) randomly. This is a key part of the randomised controlled trial (RCT).
Randomization in clinical trials means that each participant has an equal chance of being in any of the arms of the trial. It is an important method to reduce the risk of bias in the outcomes of the trial.

RANDOMIZED CONTROLLED TRIAL

A randomized controlled trial is a trial in which people are allocated at random (by chance alone) to receive one of several clinical interventions such as a new medicine. One of these interventions is the control group, for example a placebo may be given, no intervention at all, or the current best treatment available. This study is one of the simplest and most powerful tools in clinical research.

RANDOMIZED PARTICIPANTS

Participants in a trial who have been randomly (by chance) assigned to one intervention arm or another of that trial. Practical considerations, such as missing data over time, may lead to some participants not being included in the final analysis.

RARE DISEASE

A rare disease, also referred to as an orphan disease, is any disease that affects a small percentage of the population. Rare disease are commonly defined as life-threatening or chronically debilitating diseases which are of such low prevalence (fewer than 1 in 2,000 people) that special combined efforts are needed to address them. Diseases that are statistically rare, but not also life-threatening, chronically debilitating, or inadequately treated, are excluded from this definition. A disease may be considered rare in one part of the world, or in a particular group of people, but still be common in another.
Most rare diseases are genetic so that most people show symptoms from childhood (although some rare diseases only become apparent later in life).

RECEPTOR

A specialized protein molecule on the surface of a cell that binds to specific signaling molecules (ligands), initiating a cellular response.

RECOMBINANT DNA

Recombinant DNA, often shortened to rDNA, is an artificially made DNA strand that is formed by the combination of two or more gene sequences from different species. Recombinant DNA is engineered specifically for a purpose. For example, recombinant DNA can be used to change the genetic makeup of a bacterial cell in order to make it produce insulin. Recombinant genes, and the recombinant proteins they produce, have become widely used in medicine. They offer a novel method of managing some health conditions, such as the use of recombinant insulin in diabetes.

RECOMBINANT GENE

A recombinant gene is one which has been changed by the addition and/or removal of some of its sequence. This can happen naturally or may be done artificially in the laboratory.
Natural recombination happens when the chromosomes in parents interact and exchange genetic material so that their offspring inherit combinations that are different to both parents.
Recombination is one of the important causes of genetic diversity between generations and individuals.

RECOMMENDED DOSE

The dose of a drug or therapy determined to be safe and effective for use in clinical practice, based on clinical trial data.

RECRUITMENT

Recruitment is the process used by investigators to enrol people (participants) into a clinical study. Recruitment is based on the inclusion and exclusion criteria that are documented in the study protocol.

RECURRENCE

Recurrence is the return of a sign, symptom, or disease after some time when the signs or symptoms could not

be detected. It is applied to the return of symptoms of an incurable disease. For example, the reappearance of cancer cells at the same site as the original tumour, or in another location. The risk of a recurrence depends on many factors, including the type of illness and type and/or time of treatment.

REFERENCE MEDICINE
When talking about biosimilar and generic medicines, a reference medicine is the existing medicine already on the market that biosimilar and generic medicines are developed to be similar to or copies of, respectively.

REGULATORY AFFAIRS
Regulatory affairs is a relatively new profession which developed from the desire of governments to protect public health by controlling the safety and efficacy of products in areas including human medicines, veterinary medicines, medical devices, pesticides, agrochemicals, cosmetics and complementary medicines. The Regulatory Affairs departments of pharmaceutical companies ensure that their companies comply with the regulations and laws governing medicinal products or medical devices. They are the key interface between the company and the regulatory authorities.

REGULATORY AUTHORITIES
Government agencies responsible for regulating and approving drugs, medical devices, and other healthcare products for safety and efficacy.

REGULATORY INSPECTION
Regulatory inspections are conducted by health authorities or regulatory agencies to ensure compliance with applicable regulations, protocols, and standards. These inspections are conducted to verify the integrity of the trial data, the protection of participants' rights and well-being, adherence to Good Clinical Practice (GCP) guidelines, and the accuracy of recordkeeping and documentation. Inspections may be scheduled or conducted on a random basis, and they may involve a review of trial documents, site visits, interviews with trial staff, and other activities aimed at assessing the conduct and quality of the trial.

REIMBURSEMENT
In clinical research, it is the economic compensation for legitimate expenses incurred by a participant taking part in a specific research project.

RELATIVE EFFICACY
It is the extent to which an intervention does more good than harm compared to one or more alternative interventions, when provided under ideal circumstances.

RELIABILITY
The reliability of a measurement or tool is how consistent it is. A reliable measurement or tool will give the same result when repeated at random in the same patient or sample. In clinical trials, reliability is an important consideration in the choice of primary outcome measures (such as an improvement in certain symptoms). The reliability of measures should be formally assessed during the design of clinical trials. Reliability is different to validity, which is the extent to which a measurement measures what it is supposed to.

REPEATED-DOSE TOXICITY
The assessment of the potential harmful effects of a substance when administered repeatedly over a period, typically in animal studies.

REPRODUCTIVE TOXICOLOGY
Reproductive toxicology investigates the negative effects of a medicine that interfere with normal sexual function and fertility in adult males and females. Such negative effects include adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring.

REPURPOSING
Medicine repurposing is taking an existing medicine and seeing whether it can be used as an effective treatment for another condition.

RESPONSE VARIABLE
A response variable is a measured outcome within a trial which can be influenced by other factors. For example, a trial might test if a new medicine is effective at reducing a certain heart disease symptom. In this

case, the reduction in this symptom will be measured and this measurement will be a response variable (also known as a dependent variable). In contrast, the new medicine is known as the independent variable, which is tested to determine if it has caused a change in the dependent variable.

RETENTION
Trial retention refers to the ability to keep participants engaged and involved in a clinical trial from the beginning to the end. It involves strategies to prevent dropout or loss to follow-up, ensuring that participants complete the study according to the protocol requirements.

RETROSPECTIVE CASE CONTROL STUDY
A retrospective case control study is one that uses existing data to compare two groups. For example, people who have developed a disease might be compared with a group of people who have not. The researcher will look at whether there is any difference in the two groups in their previous exposure to possible risk factors. This type of study is useful when studying risk factors for rare diseases, and is often used to create new hypotheses which can then be tested.

RISK
Risk is the probability of harm or injury occurring as a result of using a treatment in clinical practice or as part of a research study. The harm or injury may be physical, but can also be psychological, social, or economic. Risks may include experiencing side effects of the treatment, or taking a medication that is not as effective as the standard treatment (during a trial). In a trial, a new treatment may have side effects or risks that researchers do not expect. This is more likely in the early stages of clinical trials.
No clinical trial is risk free. Participants should be aware of both the benefits and the risks before they make a decision about whether or not to take part (see informed consent).

RISK ASSESSMENT
Risk assessment is one of the three pillars of risk management (together with safety specifications and the risk minimisation plan). It contains both routine and additional pharmacovigilance activities to characterise the safety profile of the medicinal product including what is known and not known. It does NOT include actions intended to reduce, prevent or mitigate risks.

RISK EVALUATION AND MITIGATION STRATEGY (REMS)
A Risk Evaluation and Mitigation Strategy (REMS) is used in the United States, and is similar to the Risk Management Plan (RMP) in the EU.

RISK FACTOR
A risk factor is a characteristic, condition or habit that increases a person's chances to develop a particular disease or injury, for example, physical inactivity may, over time, contribute to weight gain, high blood pressure and high cholesterol levels. Risk factors include:

- behavioural (poor diet, smoking, alcohol consumption)
- biomedical (high weight, high blood pressure)
- environmental (social, economic, cultural)
- genetic (chromosomal abnormalities)
- demographic (age, gender, ethnicity)

RISK MANAGEMENT
Risk management is a process for identifying, assessing, prioritising, and taking the appropriate action to mitigate a risk. The objective of risk management is to continuously try to ensure that the benefits of a particular medicinal product (or a series of medicinal products) exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole.

RISK MANAGEMENT PLAN
A risk management plan provides a detailed description of the activities and interventions in place to prevent or minimise risks of using a medicine. Risk management plans outline how more knowledge about the safety and efficacy of a medicine will be generated, what are the risk factors for developing side effects, and how risk-minimisation measures will be monitored.
Risk management plans must be submitted by companies at the same time they apply for marketing

authorisation in the European Union, although they must be continually updated and revised throughout the medicine's lifetime. Risk management plans can also be requested by the EMA at other times, or whenever there is concern that a risk may be affecting the balance of benefits and risks for a particular medicine.

RISK MINIMISATION MEASURES

These are public health interventions intended to prevent or reduce the occurrence of adverse reactions associated with the exposure to a medicine, or to reduce their severity or impact on the patient should adverse reactions occur. Risk minimisation measures aim to optimise the safe and effective use of a medicinal product throughout its life cycle. Planning and implementing risk minimisation measures and assessing their effectiveness are key elements of risk management. Routine risk minimisation involves the use of the tools such as the Summary of Product Characteristics (SmPC), the package leaflet, the labelling, the pack size and design, and the legal (prescription) status of the product.

The majority of safety concerns may be adequately addressed by routine risk minimisation measures, but for some risks however, additional risk minimisation measures are necessary to manage risk and/or improve the benefit-risk balance of a medicinal product.

S

SAFETY
The condition of being protected against consequences of failure, error or any other event which could be considered non-desirable. The safety of a medical product concerns the medical risk to the patient, usually assessed in a clinical trial by laboratory tests, vital signs, adverse events and other special safety tests.

SAFETY PHARMACOLOGY
Safety pharmacology studies predict whether a medicine is likely to be found unsafe when administered to human populations within the therapeutic range. Safety pharmacology studies aim to prevent the use of unsafe medicines.
Normally, results from previous safety pharmacology studies and effects related to the therapeutic effects of the medicine are considered. Safety pharmacology uses the basic principles of pharmacology in a regulatory-driven process to generate data to inform benefit-risk assessments. Safety pharmacology includes a regulatory requirement to predict the risk of rare lethal events. The vigilant post-marketing surveillance (PMS) efforts of regulatory authorities are necessary to detect the existence of a rare adverse event occurrence after approval for human use.

SAFETY SPECIFICATION
The safety specification of a medicinal product is a summary of the important identified risks of a medicinal product, important potential risks, and important missing information. It should also address the populations potentially at risk, and any outstanding safety questions which may benefit from further investigation to refine understanding of the benefit risk profile during the post-authorisation period. In the RMP, the safety specification will form the basis of the pharmacovigilance plan, and the risk minimisation plan. It is one of the three pillars of the risk management plan.

SAFETY SURVEILLANCE
The ongoing monitoring and assessment of the safety profile of drugs or medical products once they are on the market.

SAMPLE SIZE
In a clinical trial, the sample size is the number of patients or observations made. There must be enough patients or observations so that differences between groups within the trial can be detected. An estimate of sample size is required and must be specified in the study protocol before recruitment starts. It is also necessary to control the probability with which a real effect can be identified as statistically significant. Too few patients or observations will mean that real effects might not be detected, or they will be detected but at a level that is statistically insignificant (a Type II error, which is directly proportional to sample size). It is just as true that it is unjustified for a medicine to be tested on too many patients.

SCALE-UP
In pharmaceutical development, scale-up refers to the transition of a manufacturing process from lab scale (typically milligrams/grams) to plant-scale or commercial scale (typically kilograms/tonnes).

SCIENTIFIC ADVICE WORKING PARTY (SAWP)
The Scientific Advice Working Party (SAWP) within the European Medicines Agency (EMA) provides scientific advice and protocol assistance to companies developing medicines. The SAWP was established by the EMA's Committee for Medicinal Products for Human Use (CHMP).
It is a multi-disciplinary group with expertise in non-clinical safety, pharmacokinetics, methodology and statistics, and in therapeutic fields for which there are frequent requests or other specific fields such as cardiology, oncology, diabetes, neurodegenerative disorders and infectious diseases including human-immunodeficiency-virus (HIV) infection. Membership includes representatives from the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), and the Committee for Advanced Therapies (CAT).
The SAWP develops integrated views on quality relating to the development of medicines non-clinical and clinical safety and efficacy relating to the development of medicines.

SCIENTIFIC ADVISORY GROUP
Scientific advisory groups (SAG) at the European Medicines Agency (EMA) provide independent recommendations on scientific /technical matters related to medicinal products under evaluation at the EMA, or any other relevant scientific issue. Scientific advisory groups are created by the EMA's Committee for Medicinal Products for Human Use (CHMP). They consist of experts selected according to the particular expertise required.

SCREENING
The process of identifying individuals who may have a particular disease or condition, often before symptoms are present, through testing or examination. In the T1D autoantibody screening, specific autoantibodies can be tested and identify T1D in its earliest, pre-clinical stages.

SELECTION BIAS
Selection bias occurs when there are systematic differences between the comparison groups in a study. For example, differences in clinical signs between the groups might lead to different disease progression or response to treatment between groups, rather than the intervention itself. Proper randomisation and/or blinding have not been achieved, which can affect the statistical analysis and internal validity of the study. Selection bias is sometimes used to refer to an error in the selection of studies for reviews. Publication bias is a type of selection bias. Confusingly, selection bias is also sometimes used to refer to systematic differences between the study group and the general population. This leads to problems with external validity.

SELECTIVE REPORTING
Selective reporting is the reporting of results from only a selection of studies. Selective reporting can lead to publication bias. For example, if a greater proportion of studies with a positive outcome are reported than those with a negative outcome, a review of publications will be biased toward a positive result.
Selective reporting can arise if, for example, an investigator, journal editor, or trial sponsor thinks that negative results (where no effect of a new medicine is found) are uninteresting or unimportant. However, the reporting of negative results adds valuable information to the body of evidence available, and can prevent new unnecessary trials being set up.

SENSITIVITY
Sensitivity (of an assay or test) is the ability of an experiment or trial to detect a difference, for instance, between two groups of participants receiving different medicines in a clinical trial.

SERIOUS ADVERSE EVENT (SAE)
An adverse event (AE) is called serious if it:

- results in death
- is life-threatening (at risk of death at the time of the adverse event, not an event which could hypothetically have caused death if it were more severe)
- requires hospitalisation or extension of existing inpatient hospitalization
- results in a persistent or significate disability or incapacity
- is a congenital anomaly or birth defect

Other events such as those requiring emergency intervention to prevent one of the serious outcomes described above might also be reported as a serious adverse event.

SERIOUS ADVERSE REACTION
An adverse drug reaction (ADR) is called serious if at any dose it:

- results in death
- is life-threatening (at risk of death at the time of the adverse event, not an event which could hypothetically have caused death if it were more severe)
- requires hospitalisation or extension of existing inpatient hospitalization
- results in a persistent or significant disability or incapacity
- is a congenital anomaly or birth defect

SIDE EFFECT
A side effect, or adverse reaction, is an unintended response to a medication. Side effects are generally regarded as being harmful, and may occur after a single dose or prolonged administration. They might result from the normal use of a medicine, or from the use of a medicine in a way unintended by the marketing authorization holder (MAH), such as taking an overdose or from the combination of two or more medicines being taken at once.

SIGNALLING PATHWAY
A signalling pathway is a sequence of steps involving several molecules in a cell or at its surface (receptors) that work together to control cell functions.
Signalling pathways are important in controlling many functions such as cell division, cell death, and the switching on or off of certain genes. They are directly linked to the cell's response. After the first molecule in a pathway receives a signal, it activates another molecule. This process is repeated until the last molecule is activated and the cell function is carried out. Abnormal activation or disruption of signalling pathways can lead to a variety of cell dysfunctions, among them cancer. Some cancer medicines have been developed to target these effects.

SIGNIFICANCE
In a clinical trial, the significance is a description of how meaningful (valid) a trial result is. When evaluating the validity of a study, one must consider both the clinical and statistical significance of the findings. A study that claims clinical relevance may lack sufficient statistical significance to make a meaningful statement. Conversely, a study that shows a statistically significant difference in two treatment options may lack clinical relevance (if, for instance, an observed effect is very small but highly consistent).

SIGNIFICANCE LEVEL
The significance level (or O± level) is a threshold that determines whether a study result can be considered statistically significant after performing the planned statistical tests. The significance level is most often set to 5% (or 0.05), although other levels may be used depending on the study. This represents the probability of rejecting the null hypothesis when it is true. For example, a significance level of 0.05 indicates a 5% risk of concluding that a difference between the study results and the null hypothesis exists when there is no actual difference.
The significance level must be stated in the trial protocol as part of the statistics section. The probability of a result being due to chance rather than due to a medicine or other intervention being studied, if the null hypothesis is true (that is, if there is really no true difference), is known as the p-value. A result is then said to be statistically significant if it yields a p-value equal to or less than the significance level and thus will not be considered a chance occurrence. This is generally written as p ‰ 0.05.

SILENCING
Silencing refers to the ability of a cell to prevent the expression of a certain gene. Methods used to silence genes are increasingly being used in the laboratory to produce therapies against diseases, such as cancers, infectious diseases, and neurodegenerative disorders by selectively turning off specific genes in diseased tissues.

SINGLE ASCENDING DOSE STUDY (SAD)
A single ascending dose study (SAD study) is a type of Phase I trial. Single ascending dose studies are usually conducted in a small number of healthy volunteers (although some trials recruit patients). The aim is to find out the safe dose range, and to look for any side effects. The initial dose given will be very small and increased gradually (in a new group of volunteers) if no or only mild side effects are seen. Researchers will also take measurements to determine how the medicine is processed in the body.

SINGLE BLIND TRIAL
A clinical trial where either the researchers or the participants are unaware of which treatment is being administered, but not both.

SITE VISIT
A visit by agency officials, representatives of the sponsor, or consultants to the location of a research activity

(e.g. a clinical trial site) to assess if the site is fully prepared for the protection of trial participants and the safe and successful conduct of the clinical trial.

SOLUBILITY
The ability of a substance (solute) to permanently dissolve in liquid to form a homogeneous solution.

SOMATIC
The term somatic is often used in biology to refer to the cells of the body, in contrast to the germ-line cells which usually give rise to the eggs or sperm. In medicine, it is a term that means (more generally) relating to the body. Somatic mutations are changes to the genes which are not passed on to the offspring. In cancer genetics, somatic mutations specifically refer to mutations arising in tumors (which are not present in healthy tissue). Such mutations are often responsible for driving the growth of tumors.

SOMATIC CELL NUCLEAR TRANSFER
In genetics and developmental biology, somatic cell nuclear transfer (SCNT) is a laboratory technique for creating an embryo from a body cell and an egg cell. The technique consists of taking an egg cell lacking the nucleus and implanting a donor nucleus from a body cell. It is used in both therapeutic and reproductive cloning.

SOMATIC-CELL THERAPY MEDICINE
A somatic-cell therapy medicine contains cells or tissues that have been manipulated to change their biological characteristics, and subsequently reintroduced into patients. These cells or tissues can be of autologous, allogeneic, or xenogeneic origin (cells obtained from a donor of a different species). The aim with somatic-cell therapy is to cure, diagnose, or prevent diseases.

SPECIFICITY
Specificity (of an assay or test) is the ability of an experiment or trial to correctly detect only the particular effect being studied, for instance, a difference in symptoms between two groups of participants receiving different medicines in a clinical trial. If a trial is not specific enough, it will give a false positive result (Type I error).

SPONSOR
The sponsor is the individual, company, institution or organisation which takes responsibility for the initiation and management of a clinical trial. The financing of a clinical trial may come from the sponsor, but can also come from a third-party. The organisation of a clinical trial is particularly complex because important aspects of the trial are not under the direct control of the sponsor.

STABILITY
Stability is the ability of a substance to remain unchanged. Changes may occur due to the environment that the substance is in, e.g. being exposed to sunlight or water, or being in the body. Changes may also occur due to chemical and biological processes found inside the substance.

STAGE
A specific phase or period in the progression of a disease or the development of a treatment.

STANDARD DEVIATION
The standard deviation is a measure of the amount of variation within a data set. If all values in a data set are very close together, the standard deviation will be close to zero. In such cases, the data points will all lie close to the mean (average). A high standard deviation indicates that the values are much more spread out. The standard deviation is normally included when clinical trial results are reported because it provides a (rough) guide to statistical significance. Take, for example, a clinical trial in which the observed symptom reduction is greater than one would expect if the medicine had no effect. The difference (between the observed result and what one would expect if the medicine had no effect) would generally have to be greater than two times the standard deviation to be regarded as statistically significant.

STATISTICAL ANALYSIS PLAN SAP)
A statistical analysis plan (SAP) describes the planned analysis for a clinical trial. It contains the necessary details so that is can be followed and reproduced, providing clear and complete templates for each analysis.

STATISTICAL INFERENCE

Statistical inference is the process of drawing conclusions about a population through statistical analysis from a sample of that population.

For example: In clinical trials, hypothesis testing is a means of drawing conclusions on the effect of the medicines under study on the population that the sample of trial participants was drawn from. For instance, the null hypothesis would state that the medicine being studied does not affect symptom reduction while the alternate hypothesis would state the opposite. Statistical inference from the trial data will allow researchers to reject the null hypothesis if the analysis indicates a statistically significant effect.

STATISTICAL SIGNIFICANCE

Statistical significance is a fundamental aspect of hypothesis testing. In any experiment using a sample from a population (for instance, a sample of patients with a particular disease) there is the possibility that an observed effect may be due to differences between the sample and the whole population (sampling error) rather than the medicine under study. A test result is called statistically significant if it has been predicted as unlikely to have occurred by sampling error alone, according to a threshold probability: the significance level. Statistical significance does not imply importance or practical significance. For example, the term clinical significance refers to the practical importance of a treatment effect. Researchers focusing solely on whether their results are statistically significant might report findings that are not relevant in practice. It is always prudent to report an effect size along with p-values. An effect size measure quantifies the strength of an effect, and makes it easier to draw conclusions on the practical implications.

STATISTICS

Statistics are a mathematical methods of describing and drawing conclusions from data. Statistics are an essential part of the medicines development process at multiple stages.

STEM CELLS

Stem cells are undifferentiated (unspecialised) cells that can transform into specialised cells and can divide to produce more stem cells. They have the potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as an internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. There are two types of stem cells: Embryonic stem cells, found in the early stage of embryonic development, can differentiate into all the specialised cells of the body, such as muscle cells, red blood cells, and nerve cells. Adult stem cells, which are found in some adult tissues, can act as a repair system for the body.

STEM CELL THERAPY

Stem cell therapy, also known as regenerative medicine, is the use of stem cells to treat or prevent a disease or condition. Stem cells grown in a lab are manipulated to specialise into specific types of cells, such as heart muscle cells, blood cells or nerve cells. The specialised cells can then be implanted into a person. For example, if the person has heart disease, the cells could be injected into the damaged heart muscle. The healthy transplanted heart cells could then contribute to repairing defective heart muscle.

STRATIFICATION

In clinical trials, stratification is the separation of patients or the analysis of results based on something other than the treatment given.

Stratification has two different meanings. In its first meaning, it describes the natural distribution of patients into subgroups. For instance, patients may be stratified by age, disease severity, or biomarkers.

In its second meaning, stratification controls the random allocation of people to the different groups in a trial. Stratified randomisation is used to ensure that equal numbers of participants with a characteristic thought to affect response to the intervention will be allocated to each group in the trial.

STRATIFIED MEDICINE

Stratified medicine is based on the identification of subgroups of patients that differ in their mechanisms of disease, their susceptibility to a particular disease, or in their response to a medicine. The aim of stratified medicine is to offer the treatment that is most likely to give benefit, or to avoid an adverse reaction. Personalised medicine takes this approach a step further by using targeted medicines and also taking information such as the patient's genotype and lifestyle into account when deciding on the best treatment.

STUDY MEDICATION
The study medication comprises the medicinal product(s) being given to participants in a trial (including a placebo). This also includes products already with a marketing authorisation but being used, formulated, or packaged in a new way, or being used to treat a new disease.

STUDY POPULATION
The study population is the group of individuals in a study. In a clinical trial, the inclusion and exclusion criteria describe who will and will not be included, thus defining the characteristics of the study population.

SUBCUTANEOUS
This is the administration of a medicine into the layer of skin directly below the dermis and epidermis (the top layers of skin). Subcutaneous tissue has few blood vessels and so medicines administered here are for slow, sustained rates of absorption. An example is a local anaesthetic injected before suturing.

SUBMISSION
In order to market a medicine, a submission (an application) must be made to the relevant regulatory authority, for example the European Medicines Agency (EMA). Submissions provide comprehensive information about the medicine, its formulation, the trials it has undergone, its intended use, and its risks and benefits.

SUBPOPULATION
Subpopulations are groups within a population. The population might be defined by, for example, the presence of a certain disease of interest to researchers. A subpopulation within that will have additional traits, such as disease severity, or failure of previous treatments, or specific genetic traits, or belonging to a certain age group that are also of interest. Subpopulations are identified in this way to allow statistical analysis with respect to the additional traits of interest.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The Summary of Product Characteristics (SmPC) is a document approved as part of the marketing authorisation of each medicine. It is aimed at healthcare professionals and includes information such as:

- How to use the medicine
- What the medicine should be used to treat (therapeutic indications)

SURROGATE ENDPOINT
The endpoint in a clinical trial is an event such as the occurrence of a disease, or symptom, or a particular laboratory result. Once someone reaches the endpoint, they are generally excluded from further research in the trial.
A surrogate endpoint (or marker) is a measure which in itself is not the outcome that the study treatment aims to elicit. For example, blood pressure is used as a surrogate endpoint in trials because it is a risk factor for heart attacks and strokes even though in itself blood pressure might not be important for patients.
Surrogate endpoints are useful if it would take a very long time for clinical endpoints to appear. Surrogate endpoints must be proven to be valid markers of clinical endpoints when they are used in clinical trials.

SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTION (SUSAR)
A Suspected Unexpected Serious Adverse Reaction (SUSAR), is a serious adverse reaction (SAR) for which a reasonable causal relationship with the medicine use is suspected but not confirmed. Unexpected in this context means 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).

SYMPTOM
A symptom is a manifestation of disease apparent to the patient himself, while a sign is a manifestation of disease that the physician perceives. The sign is objective evidence of disease; a symptom, subjective. (source: https://jamanetwork.com/journals/jama/article-abstract/341611)

SYSTEMIC TOXICOLOGY
This refers to toxic effects caused as a result of absorption and distribution of a substance that affects the whole body rather than a specific (local) area, i.e. to an area distant from its entry point. Most chemicals that

produce systemic toxicity do not cause a similar degree of toxicity in all organs, but usually cause major toxicity to one or two organs. These are referred to as the target organs of toxicity for that chemical.

T

T-TEST
A t-test is a statistical test that helps compare whether the average values of two groups of data are significantly different from each other. It is used to obtain a measure of the difference between the means (averages) of the groups, relative to the spread of data within each group.
The t-test helps decide whether a difference in mean values between two groups is due to random chance in a sample selection.

TARGET
A biological molecule or process that a drug or therapy is designed to affect, typically to achieve a therapeutic effect.

TARGET PATIENT POPULATION
Refers to the patients the medicine is intended for.

TARGET PRODUCT PROFILE (TPP)
A target product profile is a document that describes the features of a product (such as a medicine) that a company is planning or developing. The document can include a wide range of information such as dosage, how the product will be administered (for example this could be a patient taking a medicine by mouth, or a hospital nurse giving the medicine as an injection), formulation, clinical studies, adverse reactions (unwanted harmful effects) and contraindications (situations when the product should not be used).
The target product profile is written by the company developing the treatment, and if it is begun early it can help keep their development work properly focused on the end goal. A target product profile can also be used as a basis for discussions between the company and those regulatory authorities that will assess the product for release to market.

TARGETED MEDICINE
These are medicines designed in a manner that focuses the activity of the medication in certain parts of the body. The goal of a targeted medicine is to increase the length of time that the medicine interacts with the diseased tissue in a specific area of the body and spares other parts (e.g. affecting tumor cells rather than adjacent healthy cells). The advantages of a targeted release system are the reduction in the frequency of the dosages taken by the patient, having a more consistent effect of the medicine, reduction of side effects, and reduced fluctuation in medicine levels in the body.

THERAPEUTIC ALTERNATIVES
Therapeutic alternatives are medicines that are chemically different from the one prescribed (used) but which have the same clinical effect. Therapeutic alternatives are not to be confused with generics.

THERAPEUTIC INDICATION
Therapeutic indications are a description of the disease to be treated with a medicine, and the population for which the medicine is intended. They include the specifics about the disease, and restrictions to the patient population such as age, and whether the medicine is intended for symptom relief, cure or prevention, or whether it is for diagnostic use only.
Therapeutic indications must be clearly and concisely stated within the summary of product characteristics (SmPC) document that each medicine requires in the EU.

THERAPEUTIC TARGETS
Specific molecules, pathways, or processes within the body that are the focus of therapeutic interventions to treat or manage a disease.

TOLERABILITY
The tolerability of the medicinal product represents the degree to which adverse effects can be 'tolerated' or accepted by a patient.

TOXICITY
Toxicity is the degree to which a chemical or biological substance can damage a living organism. It can refer

to harm to specific organs, tissues or cells, or to the whole organism.
Medicines development is a step-by-step process involving the evaluation of both animal and human safety information. Non-clinical safety studies (before human testing) should be able to identify potential toxic effects that might occur under the conditions of the later clinical trial.

TOXICOKINETICS
A specific type of pharmacokinetics that studies what the body does to a medicinal product at toxic doses. These studies assess how a substance enters the body and what happens to it in the body depending on the absorption, distribution, metabolism and excretion of the substance. Toxicokinetic measurements that determine the severity of toxicity are:

- Duration and concentration of substance at the site of entry
- Rate and amount that can be absorbed
- Distribution in the body and concentration at specific sites
- Metabolic efficiency and nature of the metabolites
- Ability of the substance or its metabolites to pass through cell membranes and come into contact with specific cell components (e.g. DNA)
- The amount and duration of storage of the substance (or its metabolites) in body tissues
- The rate and sites of excretion

Different dose levels used in toxicokinetics, compared to pharmacokinetics, give rise to technological changes in such factors as solubility, stability, absorption, pre-systemic clearance, protein binding, and metabolism that may be influenced by dose size, and may give rise to profound differences in the design and interpretation of studies.

TOXICOLOGY
Toxicology is the study of the toxic effects of substances on living organisms. It includes symptoms, mechanisms, treatments and detection of poisoning, especially the poisoning of people. The main criterion regarding the toxicity of a substance is the dose, i.e. the amount of exposure to the substance.

TRANSCRIBED
Transcription is the process by which genetic information is transferred from DNA to RNA (this is accomplished by an enzyme called RNA polymerase). This RNA will in turn serve as a template to create a protein.

TRANSCRIPTOME
To produce proteins, genes are first transcribed into messenger RNA (mRNA). The transcriptome represents the whole set of mRNA molecules present in a specific cell or tissue at a certain time. By analyzing the transcriptome, researchers can determine when each gene is turned on or off in a cell or tissue, how that type of cell normally functions, and how changes in the normal level of gene activity may be altered by or contribute to disease.

TRANSDERMAL
Transdermal means through the skin is a route of medicine administration to deliver a specific dose of medication through the skin and into the bloodstream e.g. transdermal patches or ointments. Examples include nicotine patches and scopolamine patches for motion sickness.

TRANSFUSION
Transfer of blood or blood components (red and white blood cells, plasma, clotting factors, or platelets) into the bloodstream intravenously.

TRANSGENIC
A transgenic organism (otherwise known as a genetically modified organism (GMO) is an organism whose genetic material has been altered. Genetic modifications are made to produce certain traits (such as disease resistance in crops) or to cause the organism to produce specific biological products (for example, bacteria have been altered in order to produce insulin for diabetes treatment, and plants have been altered to make antibodies for blood-clotting factors).
Transgenic organisms are used in the production of medicines, in new forms of medicine such as gene therapy,

and in agriculture.
Genetic modification is also a useful tool for scientists in many areas of research, including those who study the mechanisms of human and other diseases.

TRANSLATED
In the field of genetics, translation is the process by which a protein is made from messenger RNA (mRNA). During translation, an RNA sequence is read and translated into the code of amino acids, which are the building blocks of proteins.

TREATMENT EMERGENT ADVERSE EVENT (TEAE)
Treatment emergent adverse events (TEAE) are undesirable events not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment.
In medicines development terminology, an adverse event (AE) is any undesirable event that occurs after a participant officially consents to take part in a trial (and could occur before treatment begins). An adverse event may or may not be associated with the medicine under investigation, but must be documented because it happened during the trial period.
A treatment emergent adverse event (TEAE) is an adverse event that occurs only once treatment has started.

TREATMENT GROUP
In a clinical trial, the treatment group (as opposed to the control group) usually refers to the group of participants that receives the treatment under investigation. The treatment group is also known as the treatment arm.

TRIAL ARM
A trial arm is a group of participants that receives the same interventions, or no intervention, according to the study protocol. Many randomised trials have two arms, but some may have three or even more. This is decided before the trial begins.
Trials with several arms (multi-arm) allow more than one treatment to be tested at once, and can reduce the costs and time needed during clinical development. Multi-arm, multi-stage (MAMS) trials take this idea a step further and allow the recruitment of participants in a particular arm to be stopped partway through if that treatment is not producing satisfactory results. MAMS can also allow for new treatments to be added to the trial as they become ready for testing.

TRIGGER FACTOR
A stimulus or environmental factor that initiates or exacerbates a biological process or condition.

TYPE I ERROR
Type I Error occurs in statistical hypothesis testing when a null hypothesis, which is actually true, is incorrectly rejected. Type I errors are also known as 'false positives' they are the detection of a positive effect where no effect actually exists.
As a stark example, Type I errors could kill a patient - for instance, if a study incorrectly found that the standard of care was not better than the new treatment, and consequently the new treatment was given to patients, the results may be catastrophic.
Type I errors cannot be completely avoided, but researchers should decide on an acceptable level of risk of Type I error when designing clinical trials. A number of statistical methods can be used to control the Type I error rate. The methods to be sued in a clinical trial should be detailed in the study protocol or the statistical analysis plan for that trial.

TYPE II ERROR
Type II Error occurs in statistical hypothesis testing when the null hypothesis is incorrectly accepted. Type II errors are also known as 'false negatives' they are the failure to detect a positive effect where the effect does exist.
Type II errors mean that potentially valuable research goes to waste. As no positive effect is detected, research may be halted. This research may have been useful, but as no further study takes place, no harm is done to patients.
Type II errors cannot be completely avoided, but researchers should decide on an acceptable level of risk of Type II error when designing clinical trials. To reduce the risk of Type II errors to acceptable levels, the power or sample size (the number of participants in a study) can be increased.

U

UNEXPECTED ADVERSE REACTION
An unexpected adverse reaction is a harmful and unintended response to a medication which is not consistent with applicable product information or characteristics of the medicinal product.

UNIQUE DEVICE IDENTIFICATION (UDI)
The Unique Device Identification (UDI) is a unique number, or combination of numbers and letters, given to a medical device. It is in two parts: one part identifies the device the other part identifies the producer. The aim of the UDI system is to improve patient safety: it means devices can be traced and recalled more easily, and it makes counterfeiting (production of fake copies) more difficult. The UDI is given to medical devices in addition to other labelling requirements.

UNIVERSAL DECLARATION OF HUMAN RIGHTS
The Universal Declaration of Human Rights is an international document that states the basic rights and fundamental freedoms to which all human beings are entitled. It was adopted by the General Assembly of the United Nations in 1948, as a result of the experience and atrocities of the Second World War. It represented the first global expression of rights to which all human beings are entitled " regardless of nationality, place of residence, gender, national or ethnic origin, color, religion, language, or any other status. The Declaration consists of 30 articles, and a number of key principles including:

- Universality
- Interdependence and indivisibility
- Equality and non-discrimination

The declaration has been translated into law in various forms and has inspired more than 80 international human rights treaties and declarations, which together constitute a comprehensive, legally binding system for the promotion and protection of human rights.
The full text of the Declaration is published by the United Nations on its website.
https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/

UTILITY
Utility, or usefulness, is the (perceived) ability of something to satisfy needs or wants. In health economics, utilities measure the strength of patient preferences. For example, how important various factors are to patients, such as symptoms, pain, and psychological health. The impact of new treatments on those factors, and therefore on quality of life (QoL), can then be calculated. This is a common approach used by health technology assessment (HTA) bodies, which advise on whether treatments should be funded by (for example) government health departments.

V

VALIDITY
Scientific validity refers to how well a measurement, test or study measures what it is intended to measure.

VECTOR
In gene therapy, a vector is a method of delivering DNA into patients' cells. A common vector used in gene therapy is the adenovirus. A gene therapy vector must be customised to attempt treatment of a particular disorder. To be successful, a vector must target the right cells, the gene it is carrying must be activated in the patient, and it must avoid harmful side effects.

VULNERABLE PARTICIPANTS OR POPULATIONS
Vulnerable participants or populations are individuals or groups of individuals who are unable to give informed consent to take part in a clinical trial, such as children or people affected by mental health conditions, or who may come under pressure from others to take part. It also includes people whose willingness to volunteer in a clinical trial may be unduly influenced by their expectations of taking part.
If a trial is to include people from vulnerable populations, special attention should be paid to protecting their well-being, both by the investigators and the ethics committee that reviews the trial protocol.

W

WASH OUT PERIOD
In a clinical trial, this refers to a break in ongoing treatment. It is quite often used in crossover trials where a set period is defined before switching to a new medicine. In this period the levels of the previous medicine in the body and the effects should be reduced to zero.

WHOLE GENOME SEQUENCING
Whole genome sequencing (WGS) is a laboratory process that determines the complete DNA sequence of an organism's genome at a single time. Great progress in the speed at which genomes can be sequenced, in the number of genomes that can be sequenced at the same time, and in the reducing the cost of sequencing has had a huge impact on medical research and medicines development.

High-throughput genome sequencing technologies have largely been used as a research tool and are currently being introduced into clinical practice. In the future of personalised medicine, whole genome sequencing will be an important tool to guide treatments.