EGAN
European Genetic Alliances' Network

Glossary of Terms

Introduction

Clinical trials are an essential aspect of modern medical research. Describing the scope of a trial, how it is going to work and what it is trying to find out often requires the use of many technical, scientific and other specialist terminology.

This glossary brings together definitions of many of these specialist words. The definitions used are taken from authoritative publications listed at the end and they have been written by experts in clinical trial design.

The glossary is a result of collaboration between patients (the European Genetic Alliances Network (EGAN)) and the pharmaceutical industry (Roche). We welcome feedback – especially suggestions for words we may have left out. Please send these to Alastair Kent: (alastair@gig.org.uk).

Alastair Kent
President EGAN

Chapter 1: General Terms

A

Acquis Communautaire

The acquis communautaire comprises the common set of laws and acts adopted by the European Union since the outset. It is, in some way, the contract to which the EU-25 Member States subscribe and represents an estimated total amount of 80,000 pages legislation.

Amino acids

The basic structural units of **proteins**; organic molecules capable of undergoing a wide range of biochemical reactions, most notably reactions in which they bind to each other to form long chains.

Despite their tremendous diversity, proteins (also called polypeptides) are all composed of roughly 20 amino acids found in nature. The sequence in which amino acids are arranged in a protein molecule is determined by **genes**. Ten of the naturally occurring amino acids, known as essential amino acids, cannot be made by the human body in adequate amounts or at all, and therefore have to be obtained from dietary protein.

'Talking things through with your doctor will help you to make decisions about participating in a clinical trial'

Analysis
In chemistry, the determination of the identity and amounts of the constituents of a chemical compound or mixture.

Control of large-scale chemical and pharmaceutical manufacturing processes involves automatic monitoring of analytical data. Biological systems are employed to test the efficacy or toxicity of substances. Such systems make it possible to assess the activity or harmfulness (**toxicology**) of an active drug ingredient and to establish its "fate" in the body.

Analytical systems
Instruments supplying reliable, precise and cost-effective diagnostic information; they help increase laboratory efficiency and often contribute to major improvements in treatment outcomes.

Animal experiments
Unfortunately, preliminary experiments on animals are absolutely essential in order to determine the possible effects and side effects of chemical compounds in humans. They provide invaluable information on the desired action, distribution and biotransformation of substances in individual organs and, in particular, on their possible harmful effects. It would be irresponsible to test a substance in human beings without first testing it in carefully designed animal experiments.

Antibiotics
A collective term for antibacterial substances, including natural metabolic products of bacteria, fungi, algae, lichens and higher plants and their synthetic or semisynthetic derivatives (a product originated from an entity).

Antibodies
Vast spectrum of special **proteins** formed by the @immune systems of higher animals in response to invading **antigens**; antibodies are also called immunoglobulins.

Antibodies, monoclonal
Identical antibodies formed by a single cell line; they can be produced artificially in large quantities and in highly pure form for use in research, diagnostic testing and therapy.

Antigen
Term denoting any substance recognised as foreign by the **immune** system and which provokes a defensive reaction by the body (immune response).

Immune responses may be directed against **bacteria**, **viruses** or parasites, but also include allergic reactions and rejection reactions to tissues transplanted from other persons (**organ** transplantation).

The term "antigen" has nothing to do with **genes**.

Antimicrobial resistance
The use of anti-microbial medicines (i.e. any substance used to kill or inhibit the growth of micro-organism, including antibiotics and other antibacterials, antiviral, antifungal and antiparasitical agents) has greatly contributed to improvements in health, in treating communicable diseases and preventing infections. However, overuse and misuse of antibiotics (especially in children with respiratory infections) have favoured the growth of resistant organisms. The emergence and spread of antimicrobial resistance has become a major public health problem, within the EU and worldwide.

ATC
Anatomic, therapeutic, chemical. International system for classification of medicines.

ATC/DDD
Anatomical Therapeutic Clinical Classification/Defined Daily Dose

'Keep talking things over – it can take time to come to a decision you're happy with'

Attrition rate
Refers to the rate of new chemical entities that are dropped out of the first three phases of **clinical** trials. For example out of 100 new chemical entities, 25% will drop out at phase I, of the 75 that remain for phase II, 52% would drop out. Of the 36 that remain for phase III, 36% would drop out at that phase, leaving about 23 of the orginal 100 new chemical entities that actually made it through the process.

B

Bacteria
Ubiquitous single-cell microorganisms.

Some bacteria are pathogens, causing diseases that can be treated with **antibiotics** and other antimicrobials. Far from being harmful, most bacteria are actually indispensable to plant and animal life. Bacteria and other single-cell organisms are responsible for a vast range of natural processes such as humus formation and the breakdown of organic wastes in sewage. The human body also harbours bacteria as permanent residents, notably the coli bacteria (*Escherichia coli*) which are part of the normal intestinal flora.

Benchmarking
Benchmarking is the search for industry best practices that will lead to superior performance.

Biosafety
The safe handling of biological agents such as microorganisms (particularly genetically modified microorganisms) and of animals, blood, blood components and human and animal secretions.

The goals are to ensure occupational and environmental safety by protecting staff from disease and preventing the release of biological materials into the environment.

Biosimilars
A new biological medicinal product claimed to be "similar" to a reference medicinal product which is submitted for a marketing authorization by an independent applicant after patent expiry for the originator product. In Europe, the term "biosimilar" is used as a short designation for "similar biological medicinal products". According to European legislation, Marketing Authorisation Applications for biosimilars must demonstrate the similar nature of the two biological medicinal products. Comparative quality, non-clinical and clinical studies are needed to generate evidence substantiating the similar nature, in terms of quality, safety and efficacy, of the new similar biological medicinal product and the chosen reference medicinal product.

Biotransformation.
Chemical conversion of a substance by microorganisms or @enzymes.

Blockbuster
Refers to a drug which generates over $1 billion in global sales.

Blood cells
Collective term for the cells circulating in the blood: leukocytes, erythrocytes and platelets.

The erythrocytes, or red blood cells, are responsible for oxygen transport, the platelets for blood clotting. Blood clotting disorders may take the form of persistent bleeding in newborn infants or following surgery or difficult births when certain coagulation factors are temporarily inactive or are produced in inadequate amounts (e.g. in the inherited disease hemophilia). A different type of clotting disorder occurs when platelets form an obstruction in the arteries (a thrombus), causing thrombosis, embolism or heart attack. The leukocytes, or white blood cells, are subdivided into granulocytes, B and T lymphocytes, macrophages and monocytes.

Bolar
In the US, the "Bolar" amendment to the Watchman-Hatch Act (1984) allows generic medicines manufacturers to use a patented product, before its patent expires, in the preparation of their marketing authorisation application. This amendment was part of the political balance reached when agreeing on measures to restore effective patent protection in the USA. In Europe, this balance was reached by limiting, in the SPC (Supplementary Protection Certificate) regulation, the effective marketing authorisation to a maximum of 15 years. Introducing a Bolar provision (also called "early working") in Europe would go against this equilibrium.

C

Cell
The cell is the basic unit of all living organisms. Some living organisms exist only as a single cell. This is the case for bacteria, as well as certain animals and plants. An average sized man contains from 60 to 100 trillion cells. Cells nourish themselves, produce energy, exchange information with their neighbours, multiply, and eventually die when their time has come.

Centralised procedure
Since 1995, medicinal products can be assessed via the Centralised procedure. Medicinal products that have been approved via this procedure are issued a marketing authorisation that is valid throughout the EU. This marketing authorisation is granted by the European Commission. The use of this procedure is compulsory for medicinal products derived from a biotechnological process. For other innovative products, such as products with a new active substance, a company can choose whether to follow this procedure or the Mutual recognition procedure. In the case of the Centralised procedure, a dossier must be submitted to the European Agency for the Evaluation of Medicinal Products (EMEA) in London.

Chemotherapeutic agents
Active pharmaceutical ingredients produced by chemical synthesis for the treatment of disease, as opposed to active ingredients of natural origin obtained either entirely by physical methods (extraction) or by biotechnology.

Cadreac
Collaboration Agreement between Drug Regulatory Authorities in European Union Associated Countries.

Informal voluntary cooperation of drug regulatory authorities of accessing countries, represented by their directors, that should help to prepare the area of drug regulation for accession to the European Union.

Committee for Medicinal Products for Human Use – CHMP
Within the European Agency for the Evaluation of Medicinal Products (EMEA), "the Committee for Medicinal Products for Human Use" is the scientific committee responsible for preparing the Agency's opinions on questions relating to the evaluation of medicinal products for human use. It is made up of 30 members nominated by the Member States.

Compulsory licensing
The TRIPS agreement provides strict conditions under which governments can allow the production or sale of a product without the permission of the patent holder (for example in cases of extreme urgency).

Counterfeit pharmaceutical (WHO definition)
(A fake medicine) which is deliberately and fraudulently mislabelled with respect to identity and/or source. The term counterfeiting can apply to both branded and generic products, and counterfeit products may include products:

1) with the correct ingredients;
2) with wrong ingredients;
3) without active ingredient;
4) with incorrect quantity of active ingredient; or
5) with fake packaging."

Cytokines
Hormone-like **proteins** which, even in minute concentrations, mediate and regulate interactions between different cells, creating an intracellular communications network.

D

DALY

Disability-Adjusted Life Year (DALY) measures overall burden of a disease by combining the year of potential life lost due to premature death and the year of productive life lost due to the disability. One DALY is one lost year of healthy life.

'Hospital staff will monitor you closely during your stay'

Data exclusivity (also referred to as Data Protection)
Pharmaceutical registration data are the proprietary (i.e. confidential) data generated by scientific research conducted to demonstrate the efficacy and safety of new medicines and submitted to regulatory authorities for marketing approval. Data protection periods refer to the period of time during which a company is able to keep its rights for clinical data related to a given medical product, without another company being able to use that data when applying for an authorisation to market a generic medical product.

Data privacy
Individually identifiable information, e.g. medical background and personal health data, that may not be disclosed or transferred inappropriately without the explicit authorisation of the individual.

Differential pricing
Sometimes referred to as "tiered pricing", "equity pricing" or "preferential pricing". They all refer to the same principle of adapting prices to purchasing power of the world's poorest countries.

Doha declaration
Refers to the "Declaration on the **TRIPS** Agreement and Public Health", adopted on 14 November 2001 at the Doha (Qatar) Ministerial conference of the World Trade Organization. It is a political commitment of all WTO members' governments to the TRIPS Agreement which further clarifies the flexibility already available under TRIPS, enabling developing countries to address national health emergencies.

DTCI – Direct-to-Consumer Information
In contrast with Direct-to-Consumer Advertising (DTCA) which is forbidden in Europe, the pharmaceutical industry considers that all patients should have the same right to truthful, accurate and easily understandable information that enables them, in consultation with their doctors, to make well-informed choices about their health. Europeans should have access to quality medicine information from all sources, including from pharmaceutical companies (see "information to patients").

E

EDL (Essential Drugs List)
The WHO Model List of Essential Drugs was developed in the 1970s to stimulate the rational availability of medicines in developing countries. Essential Drugs are those that meet the health needs of the majority of the population. They should be available at all times in adequate amounts and in appropriate dosage forms. The WHO Model List of Essential Drugs enables developing countries to indentify priorities and make their own drug selection. It is to be noted that over 90% of the essential drugs contained in the WHO Model List are off-patent and can therefore be legally copied, at virtually no cost, by generic companies.

EMEA (European Agency for the Evaluation of Medicinal Products)
London-based European Union agency which works in cooperation with the regulatory authorities of each Member State in the EU-wide drugs registration system established in 1995.

The EMEA coordinates the scientific resources made available by national authorities. New drugs are registered via a centralised procedure, with applications made directly to the EMEA. If an application is approved, the Commission issues European marketing authorisation. This procedure is compulsory for biotechnological products and optional for other innovative new medicinal products. The EMEA has two scientific committees, the Committee for Proprietary Medicinal Products (**CPMP**) and the Committee for Veterinary Medicinal Products (CVMP). Once products have been authorised, the EMEA continues to supervise them by measures such as inspections of manufacturing sites and monitoring of side effects. The EMEA also contributes to the development of European and international harmonisation, in particular within the framework of the EU-Japan-US tripartite International Conference on Harmonisation (ICH).

Enzymes
Proteins which act as biocatalysts in living **cells**, initiating and accelerating a wide variety of reactions, including metabolic processes.

EPAR
European Public Assessment Report - Reflects the scientific conclusion reached by the Committee for Medicinal Products for Human Use (CHMP) at the end of the centralised evaluation process and provides a summary of the grounds for the CHMP opinion in favour of granting a marketing authorisation for a specific medicinal product.

Epidemic
A widespread occurence of a disease affecting many persons simultaneously in a community or area.

Epidemiology.
The study of the distribution of diseases or of particular symptoms (in specific geographical areas, population groups or periods).

Escherichia coli
Abbreviation: *E. coli*. Nonpathogenic intestinal bacteria in humans. Laboratory strains of these bacteria are used to produce recombinant **proteins**. The most commonly used strain is K12, which is unable to survive in the human gut as a result of various defects, and can only grow under controlled laboratory and production conditions.

F

FDA
Abbreviated name of the Food and Drug Administration, the US drug regulatory authority. The FDA sets important standards and issues regulations for international pharmaceutical companies. These include requirements for genetically engineered medicinal products.

Folic acid
(pteroylglutamic acid). A vitamin occurring in food in several forms, which the body converts into various derivatives.

Folic acid deficiency may be the consequence of disease or treatment with certain drugs and may also occur during pregnancy. Abnormalities in the production of blood cells are the main clinical sign of deficiency. The hematological changes associated with folic acid deficiency are similar to those encountered in vitamin B12 deficiency, and patients are often deficient in both vitamins. Folic acid deficiency during pregnancy can have serious consequences for the unborn child. Numerous studies have shown that the risk of neural tube defects in newborns (spina bifida) can be substantially reduced by taking a folic acid preparation during pregnancy. For this reason, folic acid supplementation during pregnancy is recommended by the FDA.

Formulation
Science of preparing drugs in appropriate dosage forms. Correct formulation is essential for efficacy and the prevention of adverse reactions. It also affects the shelf-life of drugs. The term "bioavailability" is used to designate the total effect of dosage form, active ingredient and excipients on the absorption and fate of the drug in the body (**generics**, **counterfeit** drugs).

G

GATT (General Agreement on Tariffs and Trade)
A comprehensive free-trade treaty signed in 1947 by 117 nations, including almost every developed country.

The goal of GATT has been to promote global economic growth by encouraging and regulating world trade. Among other things, member countries are required to treat all other member countries equally in the application of import and export tariffs, offer basic copyright protection to authors from member countries, consult with each other about trade matters and attempt to resolve differences in a peaceful manner. GATT created an international regulatory body known as the World Trade Organization (WTO) to enforce compliance with the agreement.

Generic names

Designations assigned to chemical compounds.

In science chemical compounds are represented schematically by their structural formulas and in writing by their full chemical names. Both types of description are unsuitable for daily use because of the need to draw the formulas and because the length and complexity of the chemical names make them unpronounceable and difficult to remember. For this reason shortened generic names have always been given to chemical compounds. With this practice a need to systematise these names and give them an official status emerged. Various countries have an official body which assigns and publishes generic names. These are then known as International Nonproprietary Names (INNs). The international use of generic names is governed by the World Health Organization (**WHO**). The first step is to publish the proposed generic names. If no objection is received within four months, they are given the official status of recommended INNs. In the United Kingdom generic names of active pharmaceutical ingredients are termed British Approved Names (BANs), and in the United States US Adopted Names (USANs). The distinction between generic name and trademark is an extremely important one. Generic names refer to the active ingredient of a branded pharmaceutical product only and not to the product itself. A branded pharmaceutical is a ready-to-use, precisely measured and defined dosage form containing numerous other substances (such as carriers, stabilisers and coatings) in addition to the active ingredient. The product is identified by its trademark. Trademark and generic name must never be used synonymously.

'Data gathered during the trial will be used to inform future treatment plans'

Generics
Term applied to "copies" of brandname drugs.

After the **patent** on a brandname drug has expired, other pharmaceutical companies can start to copy it using the extensive documentation filed with the authorities by the original discoverer and manufacturer. If the chemical and pharmaceutical quality of the generic is identical to that of the original product, the authorities will grant marketing authorisation without demanding **clinical trials** to ascertain its side effects profile and efficacy. This means that generic manufacturers, which are mostly specialised companies geared to the needs of their domestic markets, have virtually no research and development costs and can sell their products at considerably lower prices than the original manufacturer.

In many countries the health authorities encourage generics for economic reasons because they provide short-term relief for healthcare budgets. Generics make no contribution to medical progress, however.

Granulocytes
Cells of the innate, non specific immune system.

Like the **lymphocytes**, they are a type of white **blood** cell. By far the most important subgroup of granulocytes are the neutrophils, or neutrophilic leukocytes, which mainly destroy bacterial pathogens. A lack of neutrophils, as can occur after chemotherapy for cancer, can lead to life-threatening infection.

H

Health
According to the World Health Organization (WHO), the "state of complete physical, mental and social well-being".

So simply defining health in terms of the absence of illness and ailments is incomplete. The UN's Universal Declaration of Human Rights states that health is a basic right. According to the WHO, health promotion refers to those measures designed to modify and promote individual behaviour and living conditions in a positive sense. Healthcare includes all those public and private institutions involved in preventive healthcare and disease management. The prevention, diagnosis and treatment of disease are closely interlinked. The links will be made even closer through integrated healthcare solutions that target the medical needs of individual patients.

Health outcome
Changes in health status (mortality and morbidity) which result from the provision of health (or other) services.

Health outcomes research
Refers to a discipline/methodology to assess the value added - including direct, indirect and intangible benefits - of a particular medicine. Industry considers that such considerations (also referred to as "pharmacoeconomics" or "cost-effectiveness studies") are not appropriate in the marketing approval process which must focus solely upon quality, safety and efficacy.

HMO (Health Maintenance Organization)
In the USA this is a health plan that is also involved in how your health care is delivered. Managed care refers to health plans coordinating your health care with you and the providers that participate in the health plan. HMOs are the most common type of managed care.

Hormone
A hormone is a molecule produced by a gland or tissue. Usually transported by the blood, a hormone affects an organ or other tissue located at a distance. For example, the pancreas produces insulin, which regulates the level of sugar throughout the organism. Hormones are "messengers" that, in concert with the nervous system, coordinate the activities of billions of cells in the human body.

Hybridomas
Hybrid cells used in the production of monoclonal antibodies.

Hypnotics
Drugs for the treatment of sleep disorders.

The various types of sleep disorder include difficulty falling asleep (sleep onset disorder), inability to sleep through the night (broken sleep), premature awakening or combinations of these. Sleep disorders may be caused by illness but are more often due to external factors, aging or mental stress. Most sleep disorders are transient, disappearing once their causes have been eliminated. For this reason every effort should be made to identify any underlying factors. Treatment with a hypnotic can be a useful temporary supporting measure.

I/J

Immunoglobulin (Ig)
Term covering various classes of proteins that function as antibodies: IgA protects the surfaces of mucous membranes against pathogens. IgD influences the way lymphocytes function. IgE protects against intestinal parasites but also contributes to many allergy symptoms.

Incidence
The number of new patients affected by the disease per annum.

Indication
The reason or circumstances that justify a particular medical measure after an assessment of the relative risks and benefits. (A contraindication is the opposite, i.e. a reason or circumstance that rules out a particular measure.) In the case of drugs, an indication is a disease or condition for which a particular preparation is thought to be an appropriate treatment.

INN
When a molecule is shown to have some useful activity, it is given an international non-proprietary name (INN), based on internationally agreed rules, which is submitted for approval to a special committee at the World Health Organisation.

Innovation
Technological progress that leads to the creation of an entirely new product (product innovation) or a reduction in the cost of producing (process innovation) or an increase in the therapeutic value of an existing product for patients. Innovations can lead to new active substances, new indications for existing products or new ways of administering the same product.

International exhaustion of international property rights
A theory which is based on the territoriality of rights and implies that after the legitimate first sale of a protected good in a country anywhere in the world, the owner of the intellectual property right on this product loses his right to restrict its (re-)exportation in any other country.

In Europe, international exhaustion is not in place and the current Community-wide exhaustion regime for trademarks allows trademarks holders in the EU to ban imports of branded goods from outside the territory of the EU into the Community. The same situation prevails for patented goods.

By contrast, the EU authorities consider the European Union as a single and unified territory where protected goods can freely circulate between the Member States. Consequently, parallel import is allowed within the territory of the EU.

Interferons
It has been known for decades that humans and animals never suffer from two viral infections (viruses) – chicken-pox and measles, for example – at the same time.

Interferon from one animal species protects only cells of the same species against viral infections. The human immune system produces three types of interferon: alfa, beta and gamma (but there are more than a dozen different, though structurally very similar, alfa interferons). All have antiviral and immunological properties. They can, for a certain time, make uninfected but susceptible cells resistant to a broad spectrum of viruses. Interferons also have antiproliferative properties (inhibition of cell multiplication and tissue growth) that are of particular interest in relation to cancer. Interferon inhibits the growth of both normal and malignant cells (in vitro). Interferons are also part of a complex mechanism that regulates the activity and maturation of important cells of the body's immune system (cytokines).

IPRs (Intellectual Property Rights)
The area of law that regulates the ownership and use of creative works, including patent, copyright and trademark law. Intellectual property rights have been developed to protect creative people who have disclosed their work for the benefit of humankind from having it copied or imitated without their consent.

L

LDC (Least Developed Countries)
Developing countries are distributed under income groups : high income, middle income, low income.

Lymphocytes
White blood cells that mount a specific defence against invading pathogens; they are part of the body's immune system.

Lymphokines
Mediators of the immune response, such as interleukins and interferons.

M

Measurement units, analytical
Measurement units used in chemical analysis to investigate the composition, structure and quantity of substances contained in compounds and mixtures.

Medicinal product
Under EU law a medicinal product is defined as any substance or combination of substances presented for treating or preventing diseases in human beings or animals.

Any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product.

Millennium Development Goals (MDGs)
The Millennnium Development Goals (MDGs), adopted at the Millennium Summit of the United Nations in September 2000, call for a dramatic reduction in poverty and marked improvements in the health of the poor. The goals and targets represent a partnership between the developed countries determined to "create an environment which is conducive to development and the elimination of poverty"

Monopsomy
A situation in which the entire market demand for a product or service consists of only one buyer.

Morbidity
The relative incidence of a particular disease in a specific locality.

Mortality
Number of deaths in a given period.

Mutual recognition
Under this procedure a marketing authorisation granted by one Member State is extended to one or more other Member States selected by the applicant. This procedure applies to the majority of conventional medicines.

N

Neurotransmitters
Relatively simple chemical messenger molecules released by nerve cells (neurons); they include epinephrine, dopamine and glutamate. (Dopamine deficiency is the cause of Parkinson's disease).

NGO
Non Governmental Organisation

NMEs
New molecular entities: products (including new chemical entities (NCEs), biological products, vaccines and products of biotechnology) that have not been previously available for therapeutic use in humans and are destined to be made available as prescription-only medicine, to be used for the cure, alleviation, treatment, prevention or in vivo diagnosis of diseases in humans.

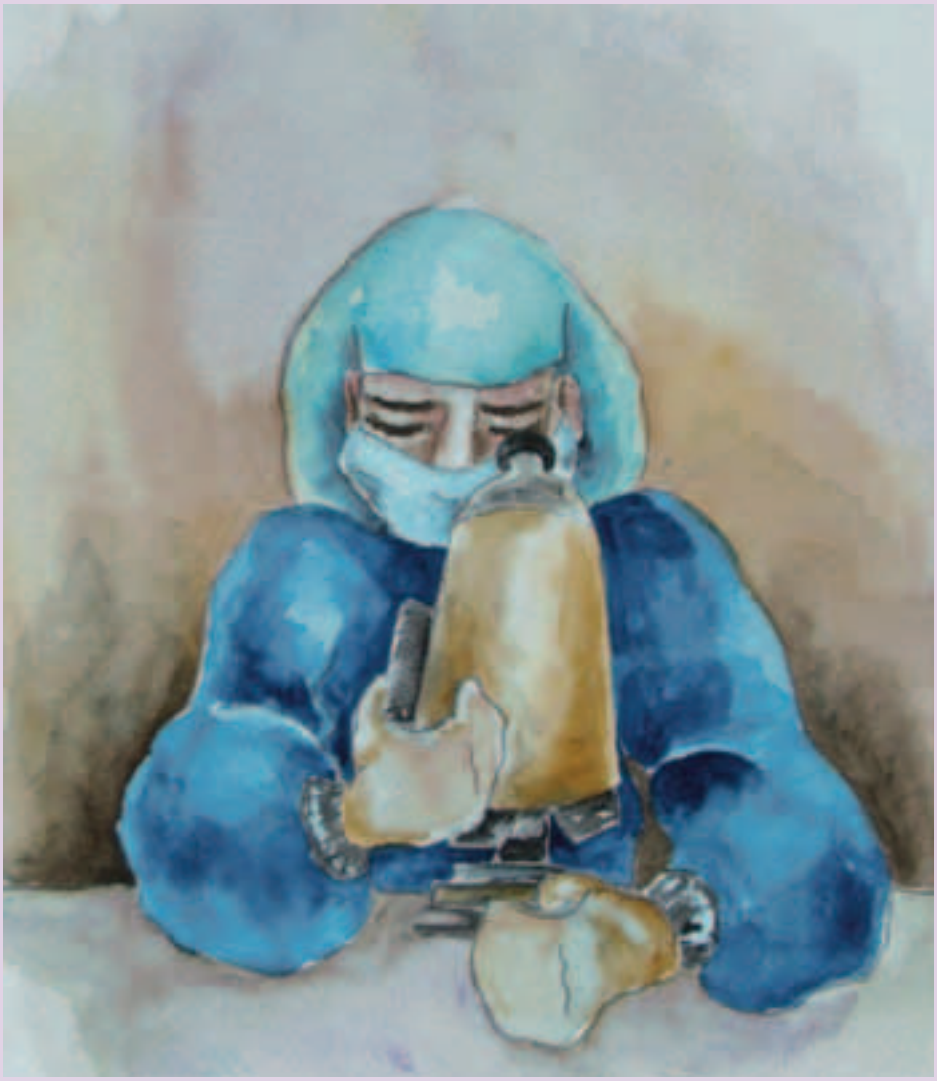
O

Occupational hygiene
Professional specialty encompassing all measures needed to protect employees from undesirable exposures to chemical, physical, biological and other physiologically active agents and influences in the workplace.

ODA
Official Development Assistance

Oncology
The study of the diagnosis and treatment of cancer. Cancer is the second most frequent cause of death in industrialised countries. Strictly speaking, it is not a single disease but rather a group of highly diverse clinical entities, all of which, however, are the result of uncontrolled (malignant) proliferation of human cells.

The increasing success of cancer therapy is the result of a multimodal treatment approach involving surgery, radiotherapy, chemotherapy and immunotherapy. In recent years immunotherapy, which specifically activates the body's own defence mechanisms, has gained in importance.



'Samples you provide will be analysed to provide further information about your condition'

Organ transplantation
Patients with organ failure find themselves in a desperate situation because of the shortage of available organs and the long waiting period for transplants. Although those with kidney failure can always be treated by dialysis, the best solution is for them to receive a "new" kidney. In the case of liver, heart and/or lung failure, transplantation is the only alternative and operations of this kind are performed in specialised clinics all over the world. Certain other organs, such as the pancreas or small intestine or sometimes several organs simultaneously, can now also be transplanted, but the necessary surgical techniques are still in the developmental stage.

Rejection of a transplanted organ, whether natural or artificial, can occur at an early stage (acute rejection) or after a long process which destroys the organ over a period of years (chronic rejection). Most patients who receive an organ transplant have to take medication for the rest of their lives to protect the organ from rejection by their own body. This is achieved by means of drugs, often very aggressive ones, which suppress the immune system, making the patients more susceptible to other diseases and to a series of severe side effects. For patients unfortunate enough to lose a transplanted kidney, there is always the fallback of dialysis; but if the transplanted organ is a vital one such as the heart, lungs, liver or pancreas, the only resort is a second transplantation. Drugs which can protect such patients against transplant rejection are of incalculable value.

OTC (Over the counter)
A medicine available without a prescription.

Outpatient care
Medical services that are provided without the need for an overnight stay in a hospital, such as through an ambulatory care clinic or emergency department.

P

Pandemic
Disease affecting persons over a wide geographical area (extensively epidemic).

Parallel trade
Parallel trade is the purchase of goods at low prices in one country and the subsequent resale of those goods at higher prices in another country.

Patent
A patent is an exclusive, but temporary, right granted to an inventor or their successors. It prevents others from exploiting the invention unless they have the patent owner's consent. Exploiting an invention includes making, using, selling, or importing it. Patents provide protection only for a limited time (normally 20 years). The patent owner also can let others use it. For example, he or she can grant a licence for an appropriate fee.

Pathogen
A pathogen or infectious agent is a biological agent that causes disease or illness to its host.

Pharmaceuticals
Collective term for products intended to restore health or prevent disease.

Originally made up by pharmacists, most pharmaceuticals are now manufactured industrially. One possible definition might be: "Products of chemical or biological origin which are intended or purported to have a medicinal effect in man or animals, and which are used especially for the detection, prevention or treatment of diseases, injuries or disabilities. " The manufacture and sale of pharmaceuticals are subject to strict statutory controls in virtually all countries (registration).

'On arrival, staff will help you settle in and prepare for treatment'

Pharmacoeconomics

A science which helps determine what benefits a new drug offers to offset its costs.

As a result of the growing cost pressure on healthcare providers, pharmacoeconomic research has steadily gained in significance.

Pharmacoeconomic research identifies and quantifies all relevant costs and consequences of a course of treatment and compares these with the existing standard. By "consequences" we mean the effects of the treatment, wanted and unwanted, as well as the usage of resources it entails. This makes it possible, for example, to ascertain whether an ostensibly high-cost medicine could save even greater costs in the long run, because it would reduce the length of hospital stays.

In most countries, pharmacoeconomic data are not required to obtain approval for a drug. However, this information is valuable and in some cases a prerequisite for inclusion on the drug reimbursement lists maintained by health authorities, health insurers and managed-care organisations.

Prevalence

The percentage of population which is affected by a disease.

Primary care

The "medical home" for a patient, ideally providing continuity and integration of health care. All family physicians and most pediatricians and internists are in primary care. The aims of primary care are to provide the patient with a broad spectrum of care, both preventive and curative, over a period of time and to coordinate all of the care the patient receives.

Production, biotechnological

Biotechnological production processes, especially alcoholic fermentation (beer brewing, winemaking etc.), are thousands of years old and widely used.

As a rule, biotechnological reactions and syntheses rely on the enzymatic mechanisms of microorganisms which are able to produce the desired products, in the form of metabolites, better and more cheaply than complicated chemical syntheses can.

Production, pharmaceutical

To make sure patients receive exactly the right dose, active drug ingredients for oral use are supplied in solid dosage forms (e.g. tablets or capsules) or in syrup or drop formulations, topical agents are available in ointment form, and agents for intravenous use are administered as sterile solutions from an ampoule or infusion bottle (formulation).

The task of pharmaceutical production is to formulate pure active ingredients as one or more of the presentations just mentioned, and, at the end of the production process, to package them as finished drug products (packaging).

Product safety
The pharmaceutical industry has the responsibility of developing products – medicines – that are safe to use and of monitoring them for the duration of their market life.

The term "safety" is used here in its widest sense and includes identifying and taking action to minimise potential risks as well as guarding against incorrect use and regularly monitoring stability.

Protease
Enzyme which cuts certain other proteins into shorter pieces. Such "protein scissors" can either break down proteins (e.g. pepsin in the gastrointestinal tract), activate them (e.g. thrombin in blood clotting) or cleave large polypeptides into smaller peptides (e.g. HIV protease, AIDS).

'You will be given lots of information to keep. Make sure you take the time to read it carefully and ask about anything you're not sure of'

Proteins
Proteins are formed by connecting much smaller molecules, amino acids, into a chain. Some proteins contain a few tens of amino acids while others are made of thousands. Each protein has a characteristic structure that depends on the order of its amino acids and the manner in which the chain folds in space. This structure determines the function of the protein: transport function (haemoglobin transports oxygen by way of the blood), defence against microorganisms (antibodies), hormonal activity (insulin, adrenalin, etc.), activation of biochemical reactions within cells (enzymes), and many others.

Public health
Public health is covered by Article 152 of the EC Treaty, which was introduced by the Treaty of Maastricht. This article states that Community action is to focus on the prevention of illnesses, including drug addiction, by promoting research into their causes and their transmission, as well as health information and education. The Treaty of Amsterdam reinforces these objectives by requiring that the definition and implementation of all Community policies and activities ensures a high level of human health protection. Under Article 152 action towards these ends may involve Community measures, complementing action by the Member States. But the main approach should be to encourage cooperation between the Member States, in line with the subsidiarity principle.

Psychotropic drugs
Pharmaceutical agents that act on mental functions by modulating nerve cell activity in the brain.

They are used primarily in the treatment of psychiatric or psychosomatic disorders. Three main types of psychotropic drug are distinguished: Neuroleptics (also called antipsychotics or major tranquillisers), which have a strongly sedative effect, are used to treat psychotic and highly agitated patients.

The first antidepressants appeared in 1957. Minor tranquillisers or anxiolytics are psychotropic drugs used primarily in the treatment of anxiety and tension.

R

Reagents, diagnostic
Products and ancillary supplies used in laboratory diagnostics to detect – both qualitatively and quantitatively – the most minute pathological changes in the composition of body fluids, and occasionally stool and tissue specimens.

Reference pricing
The practice of setting the price and/or reimbursement level of medicines according to the price set in other EU Member States. Such practice undermines price competition and jeopardizes incentives for innovation and R&D. Mixing patented and off-patent medicines in the same category of reference pricing is even worse because it prevents price competition both among generics and branded medicines, rewards imitation, and penalizes innovation.

Research expenditure
The greatest challenges in pharmaceutical R&D are posed by the relatively low success rate – only 11 percent of candidate drugs selected for clinical testing actually make it onto the market – and also by the long development times.

Restriction enzymes
Enzymes obtained from bacteria that cleave DNA molecules at specific sites. They are important tools in molecular biology, particularly genetic engineering.

Retinoids
A collective term for vitamin A and its derivatives.

The name comes from retina (the layer of light-sensitive cells at the back of the eyeball). The retinoids include very effective drugs for acne and other severe, in some cases disfiguring, skin diseases (dermatology).

Rx
Prescription medicine (in the US).

S

Secondary care
Secondary care is the term for care in hospital.

Serendipity
The faculty of making fortunate discoveries by accident.

SITC
Standard International Trade Classification.

SMEs
Small and medium size enterprises.

SmPC (Summary of Product Characteristics)
In order for a medicinal product to be evaluated either by the competent authorities of Member States or by the EMEA, a company must submit a dossier. This dossier, which in terms of content and presentation must comply with current European guidelines (Directive 65/65/EEC amended by Directive 83/570/EEC), comprises of four parts. The first part contains administrative information and a summary of the dossier, which includes the Summary of Product Characteristics. In European jargon, this information is usually referred to as the SPC or SmPC, which forms an intrinsic and integral part of the marketing authorisation.

SPC (Supplementary Protection Certificate)
The SPC applies to pharmaceutical products and was brought into effect by Regulation in the European Union on January 2 1993. The SPC has a maximum term of 5 years to give a maximum effective patent life of 15 years from the date on which a product is authorized for first marketing in a EU country.

Subsidiarity principle
It is a fundamental principle of European Union law. According to this principle, the EU may only act (i.e. make laws) where member states agree that action of individual countries is insufficient. The principle was established in the 1992 Treaty of Maastricht, and is contained within the proposed new Treaty establishing a constitution for Europe.

T

Toxicology
A subdivision of pharmacology dealing with the effects of poisons on the body.

In any drug treatment the desired action against the disease is likely to be accompanied by other effects. These may be merely inconvenient in some cases, but highly undesirable or absolutely unacceptable in others. Pharmacologists study the desired effect of a drug on a pathological condition, while toxicologists seek to establish whether the medication produces any undesirable side effects. The fate of a chemical compound depends on whether the risk of side effects is acceptable when measured against the expected benefits.

Trademarks
A visible sign or device that indicates that a product or service originates from a particular enterprise.

Trademarks are extremely important for companies, which use them to identify their products and distinguish them from those of their competitors. Since they assure customers that a certain level of quality will be maintained, they are an important factor in marketing. For this reason a trademark may be used only by the owner or a licensee authorised by the owner.

Transparency Committee
The Transparency Committee, established under Directive 89/105/EEC (and often referred to as "the Transparency Directive"), is made up of Member State representatives responsible for the pricing and reimbursement of pharmaceuticals and advises the Commission on matters relating to the Transparency Directive.

TRIPS (Trade-Related Aspects of Intellectual Property Rights)
The WTO TRIPS Agreement is a major achievement of the GATT's so-called "Uruguay Round", which sets up minimum international standards of intellectual property rights, including patents, and for enforcement of those rights, which each member of the WTO must incorporate into its national laws.

V

Vaccine
Refers to the introduction of vaccine - attenuated or killed micro-organisms (bacteria or viruses) - into the body for the purpose of inducing protective immunity against infectious diseases. Conventional prophylactic vaccines aim at stopping people becoming infected. Therapeutic vaccines are products that stimulate the immune system of people with chronic infection to eliminate the virus from their bodies. Vaccine preparations can be natural, synthetic or derived by recombinant DNA technology.

Viruses
Minute, often highly contagious pathogens consisting of an inner core of genetic material, in the form of DNA or RNA, which is frequently surrounded by one or more protective shells (capsids).

W

WHO (World Health Organisation)
Founded in 1948 with headquarters based in Geneva, the World Health Organisation is a specialised agency of the United Nations with 191 Member States, which promotes technical cooperation for health among nations, carries out programmes to control and eradicate disease and strives to improve the quality of human life.

WTO (World Trade Organisation)
Created by the Uruguay Round negotiations and established since 1 January 1995 in Geneva, the World Trade Organisation (WTO), with a membership of 145 countries, is the only global international organisation dealing with the rules of trade between nations. At its heart are the WTO agreements, negotiated and signed by the bulk of the world's trading nations and ratified in their parliaments. The goal is to help producers of goods and services, exporters, and importers conduct their business.

Chapter 2: Terms on Clinical Trials

A

Adherence
The extent to which the patient follows medical instructions and takes prescribed medicines according to treatment recommendation. In developed countries, adherence to long-term therapies in the general population is around 50% and much lower in developing countries.

'It can take a long time for all the trial results to be collated and analysed'

ADR (Adverse Drug Reaction)
A response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy for diseases or for modification of physiological function.

Advocacy and support groups
Organizations and groups that actively support participants and their families with valuable resources, including self-empowerment and survival tools.

Arm
Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more. (See Randomized trial).

B

Baseline
[1.] Information gathered at the beginning of a study from which variations found in the study are measured.
[2.] A known value or quantity with which an unknown is compared when measured or assessed.
[3.] The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. At this reference point, measurable values such as CD4 count are recorded.
Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

Bias
When a point of view prevents impartial judgment on issues relating to the subject of that point of view. In clinical studies, bias is controlled by blinding and randomization (See Blind and Randomization).

Blind
A randomized trial is "Blind" if the participant is not told which arm of the trial he is on. A clinical trial is "Blind" if participants are unaware whether they are in the experimental or control arm of the study. (See Single-blind study and Double-blind study).

C

Clinical trial
- Studies using human subjects with the aim of determining the benefits and safety of a drug. Clinical trials or studies are planned and carried out to strict scientific and medical standards and must satisfy binding ethical and legal norms.

  By means of strict observance of the detailed experimental design (close medical supervision, in addition to detailed, mandatory test protocols) the safety of the test

subjects and patients and the quality of the results are guaranteed. Prior to the start of any clinical study, moreover, approval must also be obtained from independent ethics committees and, in most countries, from the national health authorities as well. Observance of ethical and legal norms is monitored by the ethics committees and in many countries also by the authorities, by means of independent inspections.

Every clinical trial is preceded by extensive chemical and drug formulation experiments, not least for the purpose of developing a preliminary dosage form for administering the test substance to humans and animals. Moreover, the drug is subjected to detailed animal or in vitro testing for toxicity and pharmacological effects, both desirable and undesirable (**pharmacology**, **toxicology**). In particular, the metabolites of the test substance produced in the body and their effects on important organ systems must be identified in animals before clinical trials in humans can begin. But many drugs behave differently in humans than in animals; certain effects and side effects occur only in humans and not in animals, or vice versa. Based on experience, however, hypothetical models of the behaviour of drugs within the human body can be obtained. These must be painstakingly reviewed (**pharmacokinetics**).

'Staff work together to ensure you receive the best care'

- Clinical testing proceeds in four phases.

- Except for Phase I, clinical studies are usually performed outside the drug company in hospitals and, in some cases, in specialised medical practices. The investigating physician, who is also responsible for the test subjects and patients, is required to inform them in advance of the purpose and goals of the trial and of possible effects and risks. The main concern of the investigating physician in carrying out a clinical study must always be to protect the patients from physical injury (the medical principle of "first do no harm") and respect their right of privacy (doctor–patient confidentiality). Participation in a study is voluntary and the consent of the test subjects or patients to participate must be documented by their personal signature on the **informed** consent form. Participants have the right to quit a clinical trial at any time.

  Phase I trials test for tolerance in healthy volunteers (test subjects) by the administration of gradually increasing doses until the proposed therapeutic level is attained.

- In the next step, Phase II, the therapeutic effect at various dosage levels is determined in controlled, randomised tests in a small group of patients. This permits the appropriate dosage range to be established. If the results of this step are also positive, that is, if the drug is well tolerated by patients and leads to cure of the disease or at least to alleviation of symptoms, the drug enters Phase III for broader testing. In this phase, the drug – again under controlled conditions and depending on the type of illness – is administered to anywhere from several hundred to several thousand patients to test its effectiveness under different conditions, as well as its interactions with other medications.

- Long-term treatment is carried out exclusively in Phase III, after which an application for registration is submitted to the health authorities.

- Phase IV can begin once approval has been obtained. The aim of continued testing of the medication is to discover any unusual side effects, which may not appear until a drug has been used in many more patients, and to explore possible additional uses. In any case, even after the conclusion of the clinical trials programme, the drug is subject to continuous monitoring, since side effects (but also positive developments such as effectiveness in treating other illnesses) are occasionally discovered only after prolonged clinical experience.

Community-based clinical trial (CBCT)
A clinical trial conducted primarily through primary-care physicians rather than academic research facilities.

Compassionate use
Refers to situations where a drug is provided to a patient on humanitarian grounds prior to the drug's receiving regulatory approval.

Confidentiality regarding trial participants
Refers to maintaining the confidentiality of trial participants including their personal identity and all personal medical information. The trial participants' consent to the use of records for data verification purposes should be obtained prior to the trial and assurance must be given that confidentiality will be maintained.

Control group
The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo. (See Placebo and Standard treatment).

CRO (Clinical Research Organisation)
Organisation which provides services to the pharmaceutical industry and specialised in the conduct of clinical trials.

'Staff involved in your care will meet frequently to discuss your case'

D

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

Dose-ranging study
A clinical trial in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

Double-blind study
A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome. See Blinded study, Single-blind study, and Placebo.

Drug resistance.
Ability of some microbial pathogens to withstand attack from specific antimicrobials.

E

Eligibility criteria
Summary criteria for participant selection; includes Inclusion and Exclusion criteria. (See Inclusion/exclusion criteria)

Empirical
Based on experimental data, not on a theory.

Expanded access
Refers to any of the FDA procedures, such as compassionate use, parallel track, and treatment IND that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

Experimental trial
Systematic experimentation designed to examine the biological and pharmacological effects of a substance.

In rare cases, the therapeutic effectiveness of a substance is first discovered in clinical practice; as a rule, however, it is the experimental trial that leads to the discovery of therapeutic effects.

Such experiments are carried out in vitro – that is, in the test tube, in cell cultures and in isolated organs – then in animals. The type of screening usual in the past – that is, using animals to test substances about which only rudimentary knowledge was available – is now rarely practised. To identify pharmacological and chemotherapeutic effects that are worth pursuing, a substance will first be tested in therapeutic models.

Only after comprehensive experimental testing has demonstrated the safety, as well as the desired effectiveness, of a potential new medicine can it be tested in humans.

G

GCP (Good Clinical Practice)
International ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

GLP (Good Laboratory Practice)
Internationally recognised guidelines for the design and performance of experiments in the laboratory.

Before a pharmaceutical preparation intended for use in humans or animals can enter clinical @trials, it must undergo extensive testing in the laboratory (@in vitro) and in animals (@ animal experiments, @in vivo). The same applies to food additives, cosmetics and similar products. GLP governs the way in which these tests are designed and carried out.

The aim of GLP is to ensure that every experiment is planned, carried out and documented in such a way that it can be reproduced at any time.

GMP (Good Manufacturing Practice)
Regulatory standards for pharmaceutical manufacturing.

Comprehensive monitoring of manufacturing processes is vital in the pharmaceutical industry in order to ensure that the consumer receives high-quality medicines. As a company is responsible for the products it manufactures, not a single step in the process can be left to chance. The special precautions that must be taken against possible deviations are spelled out in good practice guidelines for pharmaceutical manufacturing. The guidelines issued by the World Health Organization (**WHO**) concerning the manufacture and quality control of drugs are now recognised as the "state of the art" by over 40 countries. In 1989 the European Commission began the phased introduction of GMP, with the aim of achieving uniform regulations in all member states of the European Union.

I/J

ICH (International Conference on Harmonisation)
The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration.

Immune system
All the organs, cells, body chemicals and cell functions that together defend the body against attack by **pathogens** and other foreign substances.

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

Informed consent
The concept of informed consent (required to participate in clinical trials) is based on the principle that a physician/doctor has the duty to disclose to a patient information (e.g. potential risks, benefits and alternatives) that allows the patient to make a reasonable decision regarding his or her participation in a clinical study.

Informed consent document
A document that describes the rights of the study participants, and includes details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document. The participant then decides whether or not to sign the document. Informed consent is not a contract, and the participant may withdraw from the trial at any time.

Institutional Review Board (IRB)
1. A committee of physicians, statisticians, researchers, community advocates, and others that ensures that a clinical trial is ethical and that the rights of study participants are protected. All clinical trials in the U.S. must be approved by an IRB before they begin. 2. Every institution that conducts or supports biomedical or behavioral research involving human participants must, by federal regulation, have an IRB that initially approves and periodically reviews the research in order to protect the rights of human participants.

Intent to treat
Analysis of clinical trial results that includes all data from participants in the groups to which they were randomized (See Randomization) even if they never received the treatment.

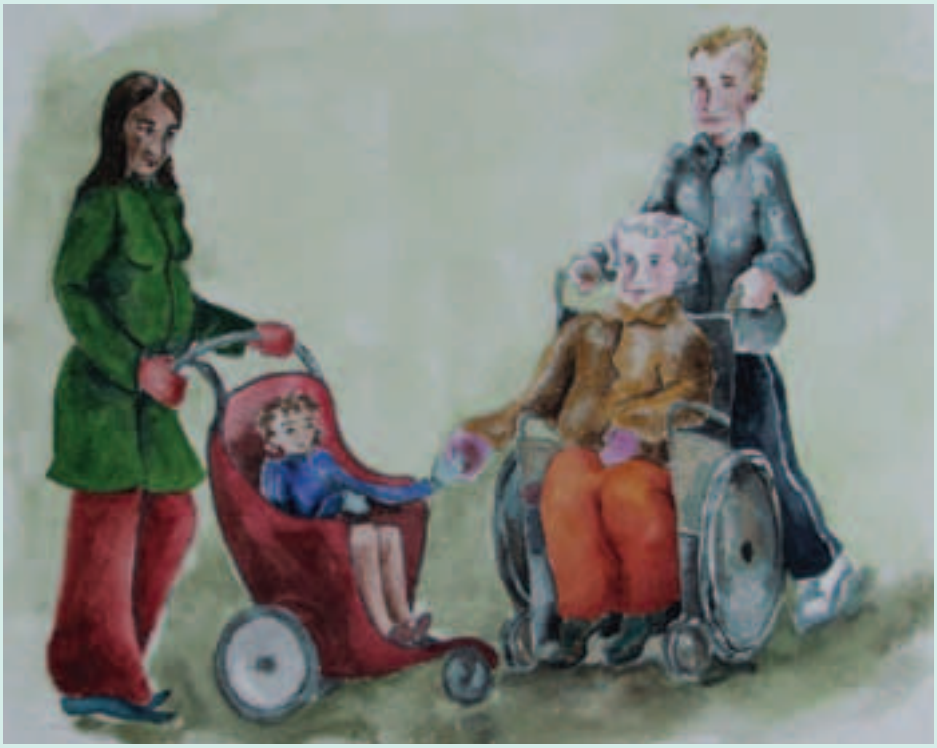
In vitro (Latin: "in glass")
Refers to an experiment conducted outside a living organism (experimental trial).

In vivo
Refers to an experiment on a living organism (clinical trial).

M

MedDRA
Medical Dictionary for Regulatory Activities Terminology. This critical medical resource, was developed by the International Conference on Harmonisation (ICH) and is owned by the International Federation of Pharmaceutical Manufacturers Association (IFPMA). By providing one source of medical terminology, MedDRA improves the effectiveness and transparency of medical product regulation worldwide.

Metabolism
Conversion of substances in the body (trial, experimental).



'Your involvement could make a real difference to future generations lives'

O

Open-label trial
A clinical trial in which doctors and participants know which drug or vaccine is being administered.

Orphan drug
A drug which only has a limited target population or which treats a rare disease thus limiting its commercial and financial potential.

P

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

Pharmacodynamics
Deals with the influence of genes on the interactions between medicines and their molecular targets.

Pharmacokinetics
Investigates the update, conversion and breakdown of medicines in the body over time. Environmental factors, diet and genetic predisposition all play a role.

Pharmacology
The study of the interactions between exogenous substances, drugs or poisons and biological systems, that is, living organisms.

The study of the effects of foreign substances on the body is referred to as pharmacodynamics; the fate of a foreign substance in the body – how it is absorbed, distributed, altered and ultimately eliminated – is known as pharmacokinetics. The special area of pharmacology concerned with the nature and effect of poisons and thus also with the toxic effects of drugs, is called toxicology.

Pharmacovigilance
Refers to the careful monitoring and continuous surveillance of the safety of an authorised medicinal product during its life on the market.

Phase I – IV
→ Clinical Trial)

PIL - Patient Information Leaflet
Provides a set of information, in a particular order, accompanying each medicine. It is usually the only source of information on how to use a medicine safely and effectively, when the patient actually takes the medicine.

PIM - Product Information Management
PIM is a project that was initiated in 1999 to develop a new way of handling product information. Its membership has been drawn from @EMEA, Member State competent authorities and **EFPIA** members. It has gone through several phases, which have culminated in the publication of the PIM standard.

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

Placebo controlled study
A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of participants, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective in treating the condition.

Placebo effect
A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change may be beneficial, reflecting the expectations of the participant and, often, the expectations of the person giving the substance.

'Large research teams are involved behind the scenes in making sure trials run smoothly'

Preclinical
Refers to the testing of experimental drugs in the test tube or in animals - the testing that occurs before trials in humans may be carried out.

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

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

Q

Quality assurance
Far-reaching concept defining the conditions required for quality-conscious working practices.

Quality assurance embraces all measures designed to ensure that pharmaceutical products meet the standards of quality appropriate to their intended use. Quality assurance, therefore, encompasses good manufacturing practice and good clinical practice, because for pharmaceutical companies the manufacture of high-quality products constitutes both an ethical commitment and an economic necessity. To achieve this goal, it is not enough to subject products to a final inspection: all employees must make quality a fundamental part of their contribution to the development, manufacture, quality control, storage and distribution of each product.

Quality control
This concerns sampling, specification and testing procedures, as well as organisation, documentation and release of products.

It is part of good manufacturing practice. Proper testing ensures that the product always meets the specifications registered with the regulatory authorities.

Quality control tests are carried out on raw materials, intermediates and endproducts in laboratories equipped with the latest instruments. Chemical, physical, biological and pharmacological assays are carried out. Quality control contributes a significant part of the analytical documentation needed for applications to the drug regulatory authorities for approval of new products. Marketed products are also subjected to stability testing. In addition to actual testing, quality control departments also approve the release of products

after review of all quality-relevant analytical and production data and monitor quality assurance activities related to purchasing, manufacture, packaging, storage and the transport of products.

Quality of life trials (or Supportive Care trials)
Refers to trials that explore ways to improve comfort and quality of life for individuals with a chronic illness.

R

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

Receptors
Protein molecules, usually found on the surface or nucleus of cells, that respond specifically to natural endogenous messengers such as hormones, neurotransmitters and cytokines, thus triggering other biological events in or on cells. Pharmaceutical research seeks to identify chemicals that bind to receptors with high specificity, thus activating or blocking them.

Registration
Before a drug that has completed development and clinical testing can be put on the market, it must first be evaluated by the authorities of the country concerned and then be officially licensed for sale through the issue of a registration certificate.

The complete documentation required for registering a new drug (known in the United States as an NDA, or new drug application) generally extends to over 100 bulky files. It contains a detailed account of all findings and results that have been obtained with the drug in laboratory tests, animal experiments and clinical trials. The documentation for the preclinical laboratory phase alone consists of several sections: a summary, data on the manufacturing process, the analytical and other quality control methods used and the chemical and physical properties of the active substance, as well as details on the finished product. The part dealing with pharmacology and toxicology contains findings from animal trials. A clinical part consolidates the experience gained with the drug during trials in healthy subjects and, especially, in patients with respect to efficacy, the incidence and nature of side effects and the drug's metabolic fate in the body.

The growing complexity of the regulations that must be observed when registration data are being prepared and compiled has led to a huge increase in the amount of time and money needed and in the number of investigations required. The task of assembling registration documentation for worldwide use is further complicated by the fact that government requirements differ widely from country to country as regards both the content and format of the application dossier. There are also differences in official procedures and the criteria

applied. In some cases the authorities allow pharmaceutical companies considerable freedom. In many countries drug registration applications are assessed solely on objective, scientific criteria, while in others the approval procedure has become a bureaucratic and often highly formalistic control system. As a result, it can take anything from just a few months (in exceptional cases) to several years for a drug to complete the registration process. Efforts are being made to harmonise approval procedures generally (ICH, good clinical practice) or at least in certain groups of countries, such as the EU (CPMP, EMEA).

Risk-benefit ratio
The risk to individual participants versus the potential benefits. The risk/benefit ratio may differ depending on the condition being treated.

S

Screening trials
Refers to trials which test the best way to detect certain diseases or health conditions.

Single-blind study
A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking (See Blind and Double-blind study).

Sponsor
Individual, company, institution or organization taking responsibility for initiation, management and financing of study.

Statistical significance
The probability that an event or difference occurred by chance alone. In clinical trials, the level of statistical significance depends on the number of participants studied and the observations made, as well as the magnitude of differences observed.

Study endpoint
A primary or secondary outcome used to judge the effectiveness of a treatment.

Study type
The primary investigative techniques used in an observational protocol; types are Purpose, Duration, Selection, and Timing.

T

Treatment trials
Refers to trials which test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.