

# Drug Discovery Glossary

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Term	Description
<b>3-[4,5-Dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT)</b>	A tetrazolium derivative used in a cell proliferation assay that detects cytotoxic compounds by quantifying cell viability.
<b>ABC transporters</b>	Alternatively called ATP-binding cassette transporters these transmembrane proteins utilise ATP binding and hydrolysis to facilitate various functions, most importantly the transfer of molecules across membranes. Defects in ABC transporters are thought to be involved in a number of diseases including cystic fibrosis.
<b>Absolute bioavailability</b>	A measure of how much drug reaches the systemic exposure circulation as determined by the areas under the curve (AUCs) from plasma concentration - time plot of a drug after administration by a non-intravenous route, compared to that following intravenous administration. $F = (AUC_{po} \times Dose_{iv}) / (AUC_{iv} \times Dose_{po})$
<b>Absorption</b>	The process whereby a drug is released from its dosage form at the site of entry to the body, before passing through biological membranes into the blood circulation to reach its site of action
<b>Absorption, distribution, metabolism and excretion (ADME)</b>	An acronym denoting absorption, distribution, metabolism, excretion; indicating the processes which determine the fate of a drug when dosed to a whole animal including man.
<b>Absorption, distribution, metabolism, excretion and toxicity (ADMET)</b>	An acronym covering absorption, distribution, metabolism, excretion and toxicity; ie the fate of, and potential adverse effects of a drug dosed to a whole animal including man.
<b>Accelerator Mass Spectrometry (AMS)</b>	A very sensitive analytical technique which allows quantitative detection (down to ng/ml) of an administered drug and/or its metabolites in biological fluids or tissues following administration.
<b>Acid dissociation constant (pKa)</b>	A quantitative measure of the strength of an acid in solution.

Term	Description
<b>Action Potential</b>	An event in various cells, including neuronal and muscle when the electrical membrane potential changes momentarily and triggers intracellular processes.
<b>Activation</b>	A response in a biological system caused by the interaction of a target biomolecule such as a protein with a cognate ligand
<b>Active Pharmaceutical Ingredient (API)</b>	The biologically active molecular constituent in a drug formulation
<b>Active transport</b>	The passage of a solute from lower to higher concentration across a membrane, against the concentration gradient. This requires energy and the assistance of a carrier protein.
<b>Activity</b>	The ability of a molecule to elicit a pharmacological effect.
<b>Acute (dosing)</b>	A dosing regimen which only needs to be given over a short period of time to treat the targeted condition
<b>Adenosine diphosphate (ADP)</b>	An important compound in metabolism and energy flow in the cell. It is phosphorylated to ATP, adenosine triphosphate, in an enzymatic process that requires input of energy. Release of phosphate from ATP provides an energy source for the cell.
<b>Adenosine triphosphatase (ATPase)</b>	An enzyme responsible for the conversion of ATP to ADP in cells releasing energy which is used for the normal functioning of the cell

Term	Description
<b>Adenosine triphosphate (ATP)</b>	A molecule which is vital for energy generation in cells. Enzymatic cleavage of one phosphate group releases energy which drives other processes in the cell.
<b>Adverse Event (AE)</b>	The observation in a volunteer or a patient in of an unexpected effect of dosing a drug which may or may not be drug-related.
<b>Affinity</b>	A measure of the strength of the binding between a ligand and a target, in this context frequently between a potential drug molecule and a receptor .
<b>Agonist</b>	A chemical which interacts with a receptor to give a positive biological response.
<b>Albumin</b>	A major plasma protein that exerts several functions and frequently binds administered drugs. One particular example is BSA, bovine serum albumin which is often used as a component in bioassays to provide some physiological relevance.
<b>Aldehyde oxidase</b>	An important metabolic enzyme present in the cytosol which operates in an NADH independent fashion. It is responsible for a range of metabolic transformations, including those of aldehydes and nitrogenous heterocycles. The latter is probably the most important in the context of medicinal chemistry and lead optimisation.
<b>Allergen</b>	A protein, usually foreign to the body which provokes an allergic response
<b>Allometric scaling</b>	A scaling factor used to compare drug-related parameters e.g exposure, kinetics, dose, from one species, e.g. the rat, to another, particularly man. It takes into account the size differences between the species.

Term	Description
<b>Allosteric inhibitor</b>	An enzyme inhibitor which does not bind at the active catalytic site. Rather, it binds elsewhere on the enzyme causing conformational changes thus inhibiting the enzyme.
<b>Allosteric site</b>	A ligand site on an enzyme which is distinct from the co-factor binding (orthosteric) or catalytic region. Inhibition kinetics of enzyme activity by binding to this site are usually uncompetitive in nature
<b>Ames test</b>	An <i>in vitro</i> test using histidine deficient bacteria to establish the mutagenic potential of test compounds
<b>Amorphous solids</b>	The lowest energy, most disordered, non-crystalline solid form of a compound. This form often has the best solubility.
<b>Amphipathic</b>	A molecule with both lipophilic and hydrophilic domains. Also termed amphiphilic.
<b>Amylase</b>	A digestive enzyme produced primarily in the pancreas and salivary glands that catalyses the breakdown of starch to smaller carbohydrates.
<b>Anabolism</b>	A metabolic process which is energy consuming and results in the construction of larger molecules from smaller fragments.
<b>Anaesthetic agent</b>	A drug which renders the patient in an insensitive state thus allowing potentially painful or invasive medical procedures to be conducted. May be local or general.

Term	Description
<b>Analgesic agent</b>	A drug which reduces or negates pain being suffered by the patient.
<b>Analogues</b>	Compounds bearing a close structural similarity with a hit or lead compound.
<b>Antagonist</b>	A compound which interacts with a receptor without initiating a biological response. Further, the binding prevents other ligands from binding to the site and exerting their natural effects.
<b>Ante-drug</b>	A drug design concept, initially developed for locally acting steroidal antiinflammatories and respiratory drugs, in which the active compound carries a group which can be readily metabolised in the bloodstream to give an inactive compound. Thus the drug action is confined to the initial location. Can be considered to be the opposite of a prodrug.
<b>Antibody</b>	A complex protein structure produced by the cells of the immune system which binds tightly and specifically to foreign proteins (antigen) entering the blood stream. It is part of the body's natural defence system
<b>Antibody-Drug Conjugate</b>	A drug in which a small molecule (often a toxic anti-cancer agent) is covalently bound to an antibody specific to proteins on the target organ. After selective binding to the organ, the drug is released to attack the tumour.
<b>Anti-cancer agents</b>	Collective terms for the various classes of drugs which are used in oncology
<b>Anti-convulsant</b>	Drugs which counter the convulsions typically seen in epilepsy and epilepsy-like conditions.

<b>Term</b>	<b>Description</b>
<b>Anti-emetic</b>	Drugs which prevent vomiting. They are particularly useful in some chemotherapeutic regimens where vomiting can severely inconvenience the patient and prevent the anti-cancer therapy being absorbed.
<b>Antigen</b>	A biomolecule foreign to the body which stimulates the immune system, and induces the production of specific antibodies.
<b>Antihypertensive</b>	A class of drugs that reduce blood pressure.
<b>Antimetabolite</b>	A design concept used especially in cancer chemotherapy whereby the drug competes with the pyrimidine or purine bases used in DNA synthesis, thereby affecting cell division.
<b>Antiviral</b>	A drug used to combat a viral infection.
<b>Apical</b>	A description of the membrane of a polarised cell such as an epithelial, endothelial cell or neuron which faces into either the lumen or the inner space of a tubular structure such as an artery or intestine.
<b>Apo structure</b>	The apo structure or conformation of a protein is one that is lacking its ligand or, in the case of an enzyme, any bound co-factor.
<b>Apoptosis</b>	The process by which a cell undergoes programmed cell death

Term	Description
<b>Apparent volume of distribution</b>	The theoretical volume of plasma (in litres) a given dose of drug would have to be dissolved in to have the actual concentration detected in the plasma after administration at that dose. $VD = \text{total amount of drug in the body} / \text{drug blood plasma concentration}$
<b>Aquaporins</b>	A family of membrane proteins that form pores in the membranes of cells.
<b>Archaea</b>	Single-celled prokaryotic organisms which differ from bacteria in their genes and metabolic pathways.
<b>Area under curve (AUC)</b>	A parameter, derived from a plot of the drug plasma concentration against time, which reflects the actual body levels after exposure to a dose of the drug. Its value depends on the dose administered, its absorption, and how readily the drug is removed from the body.
<b>Assay</b>	The procedure used for the measurement of the activities of a series of compounds, in a test system predictive of biological activity. This may involve cells, tissues or enzymes/receptors.
<b>Association of the British Pharmaceutical Industry (ABPI)</b>	A trade association of pharmaceutical companies and industry personnel formed to recommend and support agreed practices concerning the industry and to represent the industry on external decision making bodies.
<b>Attrition</b>	The loss of compounds put into development which cannot be further progressed because of discovered problems such as relative lack of activity in man, toxicity, selectivity, unacceptable side effects etc.
<b>Audit (Clinical)</b>	An independent and retrospective examination of procedures and practices followed throughout a clinical trial in order to examine the compliance with the protocol and the regulations governing the trial.

Term	Description
<b>Audit Trail (Clinical)</b>	Data established during a clinical trial which facilitates the retrospective carrying out of a comprehensive audit.
<b>Auto phosphorylation</b>	The phosphorylation of a newly translated protein resulting in regulation of its functions.
<b>Autoimmunity</b>	A serious condition in which the body's immune system incorrectly identifies proteins from the body as being foreign and mounts an attack on them. A number of diseases such as type I diabetes, rheumatoid arthritis and multiple sclerosis are thought to be autoimmune diseases.
<b>Autonomic nervous system</b>	A control system in the body which acts largely unconsciously to regulate the function of the internal organs. It is differentiated into the sympathetic and parasympathetic nervous systems.
<b>Backup</b>	A molecule with closely similar biopharmaceutical and pharmacological activities to the developmental compound for which it could be substituted in the event of the first compound showing unacceptable difficulties. It often has an unrelated structure or core.
<b>Bacteria</b>	A large domain of single-celled organisms with a variety of shapes and a length usually less than 50 micrometers. They lack organelles including a nucleus and are protected by a membrane with, in most cases, an outer cell wall. Whilst some bacteria are pathogenic others have no effects on humans and still more seem to play a protective role in the gut.
<b>Basolateral</b>	The converse of apical, i.e. the membrane of a polarised cell such as an epithelial, endothelial cell or neuron which faces the outer region of a tubular structure such as an artery or intestine.
<b>Batch</b>	A specific lot of drug product, or supply of materials for dosing or formulation whose origins can be traced to the same excipients and manufacturing process.

Term	Description
<b>Beta-lactamases</b>	Enzymes causing resistance to beta-lactam antibiotics by hydrolytic cleavage of the NH-CO bond in the four-membered ring.
<b>Bile</b>	A fluid produced by the liver, and containing numerous substances which aid digestion in the lower intestine.
<b>Binding parameters</b>	The numeric variables used to describe the interactions between ligands and proteins which help in the understanding of pharmacokinetic and pharmacodynamic properties
<b>Bioavailability</b>	A measure of the efficiency of absorption of a substance after dosing. Usually measured by analysis of a plasma concentration - time curve.
<b>Bioequivalence</b>	Two or more formulations are said to be bioequivalent when they show identical bioavailability and as a consequence exert the same biological / clinical activities. Usually used in the context of the approval of a generic medicine compared to the original branded drug.
<b>Bio-isosterism</b>	A drug design concept in which certain atoms or functional groups interact in a similar manner with their intended target, thus conveying very similar biological activities. They can therefore be substituted for one another in the search for new active molecules, and may exhibit differing drug properties such as pharmacokinetic improvements or intellectual property advantages.
<b>Biological Investigational Medicinal Product</b>	An investigational (new) product of biological origin obtained either by isolation from biological tissue or by clonal technologies. Usually a peptide or protein with a specific biological activity. Not a small molecule.
<b>Biomarker</b>	A specific biological process or molecule, the monitoring of which provides a surrogate readout of the effect of a drug on the biological system, thus providing evidence of its activity. This is particularly useful when the biomarker can more rapidly or less intrusively predict a clinical end point.

Term	Description
<b>Biomolecule</b>	Molecules produced by a living organism. Frequently but not exclusively referring to large molecules such as antibodies, proteins, lipids, nucleic acids and their derivatives.
<b>Biosimilar Medicine</b>	A biomolecule having similar clinical properties to an already registered biomedicine and for which specific registration approval procedures apply. Biosimilar molecules are often made by cloning technologies and can be of varying size from relatively small growth factors to complex molecules such as antibodies.
<b>Bipartite carrier</b>	A protein with adjacent amino acid sequences which are repeated a number of times (tandem repeats), useful for presenting antigens in the generation of antibodies
<b>Bivalent Antibody</b>	An antibody which has within its structure two (or more) sites of recognition for a specific antigen. Such antibodies cause observable effects such as precipitation or agglomeration of the complex.
<b>Blood-brain barrier</b>	The very tight complex membrane that surrounds the brain and spinal cord, and which prevents the entry of potentially toxic materials. Passage through this membrane takes place through hydrophilic pores and specific uptake and efflux transporters.
<b>B<sub>max</sub></b>	The maximum amount of a drug or radioligand that can bind specifically to a receptor or an enzyme in a tissue preparation. Usually expressed in picomoles/mg of protein.
<b>Bone marrow</b>	A flexible tissue found within bones where stem cells reside and continually provide all the cells of the blood.
<b>Bound</b>	The status of a drug attached reversibly or irreversibly to a receptor or enzyme

Term	Description
<b>Caco-2 cells</b>	A human colon carcinoma cell line suited to and extensively used for the <i>in vitro</i> study of the ability of small molecules to pass through biological membranes and therefore be able to modulate intercellular targets. Often used in comparative permeability terms to facilitate the selection of the best candidate from an active series.
<b>Calculated logP value (cLogP)</b>	An <i>in silico</i> calculation which provides an estimate of the lipophilicity of a molecule based on assigned properties of each constituent atom
<b>Cancer</b>	A set of diseases caused by the uncontrolled proliferation of cells.
<b>Candidate (molecule)</b>	A molecule selected from an active series for further study. Often used to refer to a compound selected for preclinical development.
<b>Cannabinoid receptors</b>	A small family of G protein-coupled-receptors found throughout the body which are involved in a number of sensations including appetite, pain, mood and memory. CB1 is centrally located whereas CB2 has wider peripheral distribution.
<b>Carboxylases</b>	A class of enzymes that catalyses the carboxylation of a substrate biomolecule
<b>Carrier mediated active transport</b>	The energy dependent process by which a transmembrane protein transports a drug across a biological membrane.
<b>Carrier molecules</b>	A biomolecule, for example a carbohydrate, which can combine with a drug to facilitate its transport through a cell membrane.

Term	Description
<b>Carrier prodrugs</b>	A conjugate molecule comprising an active principal attached to a carrier molecule, which after transport through the membrane is then released at the site of action.
<b>Catabolism</b>	The enzymatic breakdown of complex biomolecules with the release of energy
<b>Cell</b>	The smallest discrete functioning unit within the body. It is comprised of a phospholipid membrane surrounding the cytoplasm in which are found various organelles and a membrane enclosed nucleus.
<b>Cell assay</b>	A procedure established in order to study the mechanism of action or function of a molecule on a given cell type.
<b>Cell proliferation assay</b>	An biological test used to assess the effect of test compounds on the growth and multiplication of cells.
<b>Cell signalling</b>	The process by which binding of a ligand to a receptor on the surface of a cell initiates a cascade involving a highly organised sequence of proteins interacting with one another to transmit information from one part of the cell to another, eg using phosphorylation events.
<b>Cell surface receptor</b>	A receptor protein found on the outer membrane surface of the cell which bind to biomolecules such as chemokines and cytokines, and transmit signals as a result. There are a number of different types dependent on whether both terminals of the protein lie outside the cell, or whether one terminal is outside and the other inside and on the number of loops of the protein found in the cell membrane.
<b>Central Nervous System (CNS)</b>	A part of the nervous system of the body comprising the brain and spinal cord

Term	Description
<b>Central targets</b>	Enzymes and receptors within the central nervous system, whose interaction with a drug elicits a pharmacological response
<b>Cerebrospinal Fluid (CSF)</b>	A fluid found in the brain, spine and central nervous system
<b>Certificate of Analysis</b>	A document recording the experimentally measured compliance of a drug substance with the established analytical specification.
<b>Chaperone protein</b>	Proteins that assist in the folding and/or assembly of complex biological structures within the body
<b>Chemical antagonism</b>	A process whereby an endogenous agonist interacts with a second molecule remote from the enzyme active site, changing its structure and thereby preventing interaction and resulting in a lack of biological response.
<b>Chemoinformatics</b>	The use of information resources, such as computational databases containing structures, activities etc. of a series of compounds to better understand their biological properties and to enable predictions to be made of the activity of new compounds thus aiding the drug design process.
<b>Chemoreceptor trigger zone</b>	An area in the brain (medulla oblongata), the stimulation of which by drugs or hormones initiates a vomiting response. Particularly important in the context of reducing emetic side effects of anti-cancer drugs.
<b>Chemotherapeutic agent</b>	A drug used for the treatment of cancers.

Term	Description
<b>Chloride channel</b>	A family of transmembrane ion channels allowing the passage of chloride and other anions into and out of the cell. They play an important role in cellular and physiological homeostasis and response.
<b>Chromosome</b>	An multicomponent cellular structure which consists of most of the DNA of the organism in close contact with a histone protein, and which transmits hereditary information. In normal human development there are 23 pairs of chromosomes.
<b>Chronic dosing</b>	A dosing regimen where the drug has to administered over a prolonged period of time because of the nature of the targeted illness.
<b>Clastogen</b>	An agent which causes mutagenicity by disrupting or damaging chromosomes. It can also lead to carcinogenicity.
<b>Clearance</b>	The process whereby the body removes an ingested drug from the blood circulation. This occurs via metabolism and elimination mechanisms in specific organs, mainly liver, kidney and lungs, thus curtailing its physiological activity.
<b>Clinical Trial Authorisation</b>	Permission granted by the appropriate regulatory authority for the carrying out of a clinical trial defined by a protocol and supported by the prerequisite non-clinical data.
<b>Clinical trials</b>	Highly organised and regulated trials of new drugs both in human volunteers and patients. They are divided typically into 5 phases ( 0 to 4), with the overall objectives being to demonstrate safety, and to find the true potential activity of the new compound. In pivotal, registration enabling trials prior to marketing the drug its activity will usually be measured against a placebo and a drug already used in the target illness.
<b>Co-crystal structure</b>	The structure of a ligand bound to its target, as determined by X-ray crystallography. This shows the geometry of interaction between the two molecules and facilitates both the study of the interactive forces and the design of other ligands.

Term	Description
<b>Co-factor</b>	A chemical required for an enzyme to perform its function, for example, ATP is essential as a source of phosphate for kinases.
<b>Combination therapy</b>	The use of two or more drugs to treat a single symptom or disease.
<b>Combinatorial chemistry</b>	An (often automated) synthetic chemistry strategy to produce a large number of structurally related molecules in a more rapid and efficient manner than by using conventional linear synthetic techniques. In medicinal chemistry in combination with high throughput screening, this provides a method for the rapid identification of hit compounds.
<b>Competitive antagonist</b>	A drug which exerts no biological effect, but which competes at the receptor at the same site as the natural ligand or agonist, thus moderating their effects
<b>Competitive Inhibitor</b>	A ligand that exerts its effects on an enzyme by binding to the site normally occupied by the natural substrate.
<b>Compound Library</b>	A collection of many molecules in a screen-ready format which can provide the starting point in the search for hit molecules in a new medicinal chemistry project.
<b>Concentration-Response Curve</b>	A plot of the observed response (y-axis) as a result of the administration of a known concentrations of a drug substance (x-axis) in an assay system.
<b>Conformation change</b>	A change in the three dimensional shape of a molecule without a concomitant change in the covalent structure

Term	Description
<b>Conjugation</b>	The delocalisation of electrons resulting from the overlap of "p" orbitals
<b>Constitutive activity</b>	The ability of some receptors to produce their effects in the absence of a bound ligand. Such activity may be blocked by the presence of an inverse agonist. See also Receptor Tone
<b>Contract Research Organisation (CRO)</b>	An independent organisation engaged to carry out specific procedures on behalf of and under the responsibility of a sponsor organisation.
<b>Contractile proteins</b>	Proteins found in muscle, other tissues and cells which contract in response to various signals or stimuli.
<b>Control of Substances Hazardous to Health (COSHH)</b>	Regulations defining the handling of substances which may be hazardous.
<b>Cortisol receptor</b>	The nuclear receptor (NR3C1) , found in most cells, to which cortisol and glucocorticoids bind and exert their effect on genes whose protein products control many of the body's functions.
<b>Cyclic adenosine monophosphate (cAMP)</b>	A secondary molecular messenger regulating many intracellular biological responses.
<b>Cytochrome P450 (CYP)</b>	A superclass of oxidising enzymes containing a haem factor which are responsible for much of the metabolism of drugs. The nomenclature results from the fact that in the reduced form and complexed with CO they absorb light at 450nm.

<b>Term</b>	<b>Description</b>
<b>Cytokine</b>	High molecular weight hormones released in response to specific stimuli and having specific effects.
<b>Cytoplasm (cytosol)</b>	A clear fluid comprising the contents of a cell, between the membrane and the nucleus
<b>Cytotoxic drug</b>	A drug having a toxic effect on cells. Used extensively in the treatment of cancer but often with significant side effects due to their lack of specificity.
<b>Decarboxylase</b>	A class of enzymes that catalyses the decarboxylation of a substrate biomolecule
<b>Declaration of Helsinki</b>	Ethical regulations published by the World Medical Association designed to ensure the safety of individuals taking part in clinical trials.
<b>Dehydrogenases</b>	A group of enzymes catalysing the oxidation of substrates by the formal transfer of hydride ion to an electron acceptor.
<b>Delayed Hypersensitivity Reaction (DTH)</b>	A non-immediate symptomatic immune response to an allergen to which the subject is already sensitised
<b>Depolarisation</b>	A change in the membrane potential of a cell in which it becomes more positive either through the removal of negative charges (ions) on the inner cell membrane or the accumulation of positive charges (ions) on the extracellular surface.

Term	Description
<b>Differentiation</b>	The process whereby a cell, for example, a stem cell, changes into a more specialised cell with a more restricted range of properties and reduced plasticity.
<b>Diffusion</b>	The purely physical process whereby solute molecules move from a region of higher solute concentration to one of lower concentration.
<b>Diffusion barriers</b>	Regions within cellular and intracellular membranes that restrict the diffusion of specific proteins to distinct domains or compartments, thus controlling the function of the cell.
<b>Diffusion coefficient (D)</b>	A constant used in equations depicting the movement of materials through a medium. $D=m^2/s$
<b>Distomer</b>	Drugs containing chiral centres are often found to have different biological activities between the enantiomeric pair. The less active isomer is known as the distomer. (see also eutomer)
<b>Distribution</b>	The process whereby a dosed drug moves from the blood circulation into the various tissue compartments. It is affected by the speed of the blood flow, the nature and permeability of the biological membranes to be crossed and the affinity of the drug for specific tissues.
<b>Distribution, metabolism and pharmacokinetics (DMPK)</b>	The study of how the body processes the drug following dosage via the intended route
<b>Diversity</b>	A term to describe the range of dissimilarity within a set of molecules. Often used in the context of screening to ensure that as broad a structural range as possible of compounds is tested against a biological target. Can be quantified by, for example, a Tanimoto coefficient

Term	Description
<b>DNA (gene) transcription</b>	The initial stage of the process whereby DNA segments, ie genes, produce their respective proteins. The first step is to produce a chain of RNA complementary to the DNA sequence, which ultimately results in protein synthesis in the ribosome, following translation.
<b>DNA (gene) translation</b>	The later stage of the process whereby genes produce their respective proteins. This step involves reading of the cognate mRNA which then initiates protein synthesis in the ribosome.
<b>Dose</b>	The amount of a substance administered expressed either in absolute terms (e.g. 50mg) or in relative terms by body weight or area (e.g. 5mg.kg <sup>-1</sup> ; 2mg.m <sup>-2</sup> )
<b>Dose ratio</b>	The ratio by which a dose of an agonist has to be increased in the presence of an antagonist for the same receptor to give the same level of response
<b>Dose response curve</b>	A plot of the response of a tissue, cell, enzyme or receptor to increasing doses of an active substance, leading to a maximal response. It usually has a sigmoid shape. Non-sigmoidal curves can be caused by factors like cytotoxicity.
<b>Dosing regimens (q.d., b.i.d., t.i.d)</b>	The frequency of dosing for a drug. q.d.- daily; b.i.d.- twice daily; t.i.d.-three times daily
<b>Dosing routes (p.o, i.p., s.c., i.m., i.t., s.l., i.v .)</b>	Routes of administration for drugs. The main ones are p.o. oral; i.p. intraperitoneal (body cavity); s.c. subcutaneous; i.m. intramuscular; i.t. intrathecal (spinal column); s.l. sub-lingual and i.v. (intravenous)
<b>Double stranded RNA</b>	A helical structure, formed by two base complementary RNA strands, and found as the genetic material of a number of viruses.

Term	Description
<b>Double-blinded</b>	A clinical trial in which neither the patient nor the administering clinician know whether they are receiving the candidate drug, a comparator drug or a placebo
<b>Drug</b>	A substance which when administered to a living organism produces a beneficial biological effect
<b>Drug conjugate</b>	See 'Antibody drug conjugate'
<b>Drug elimination</b>	Processes that result in the drug and/or its metabolites being removed from the body. Usually this is via the urine or faeces, with the faeces often also containing unabsorbed, unchanged drug.
<b>Drug receptor interactions</b>	The way in which a drug binds to its specific target molecule. This is usually, but not always, a reversible non-covalent interaction.
<b>Drug target</b>	The specific receptor, enzyme, cell or tissue on which the drug exerts its biological activity
<b>Drug transporters</b>	Membrane proteins that specifically aid the movement of a drug through the cell membrane into or out of the target cell.
<b>Druggability</b>	The likelihood that a new biological target could be affected by a drug thus leading to beneficial therapeutic effects

<b>Term</b>	<b>Description</b>
<b>Drug-like</b>	A subjective assessment by the medicinal chemist of how likely a new structure is to have useful drug properties. See 'Lipinski's Rules'
<b>Dual pharmacology</b>	The effect resulting from a drug that interacts with more than one biological target.
<b>Effective dose 50</b>	The dose of a candidate drug which produces the desired effect in 50% of dosed subjects.
<b>Effective drug concentration (EC50)</b>	The concentration of a candidate drug which produces half the maximal effect in a biological test or assay.
<b>Efficacy</b>	A measure of the ability of a substance administered to have the desired therapeutic or functional effect
<b>Efflux</b>	The active transport of drugs out of cells, tissues or through membranes against a concentration gradient via transporter or carrier proteins.
<b>Electrocardiogram (ECG)</b>	A recording of the sequence of the electrical activity of the heart.
<b>Elimination</b>	Processes that result in the drug and/or its metabolites being removed from the body, usually in the urine and faeces.

Term	Description
<b>Elimination rate constant <math>K_{el}</math> or <math>K_e</math></b>	A pharmacokinetic term used to describe how rapidly a drug is removed from the body. It is equivalent to the fraction removed per unit time measured at a specific point in time. $C_t = C_0 \cdot e^{-kt}$
<b>Embryo</b>	The early stages of development of a fertilised egg. In humans this is usually taken to mean the development taking place up to the 12th week of pregnancy. (see foetus)
<b>Endogenous factors</b>	Chemicals in the body which are produced naturally within the body
<b>Endogenous mediators</b>	The intracellular proteins that transmit signals resulting from the interaction of agonists with cell surface receptors thus giving the cellular response.
<b>Endoplasmic reticulum</b>	An intracellular structure which forms a network of flattened membrane enclosed sacs or tubes, and is involved in intracellular protein transport
<b>Endothelial cells</b>	A layer of cells found on the inner wall of blood vessels and lymphatic vessels.
<b>Enterohepatic recirculation</b>	The process by which drugs and their metabolites present in the systemic circulation are eliminated from the liver in the bile into the GI tract, and then subsequently re-absorbed. This can lead to higher than expected values for bioavailability.
<b>Entropic term (<math>\Delta S</math>)</b>	A measure of the disorder in the system which along with changes in the enthalpic term gives the change in free energy in a system. Relevant when considering the binding of a ligand to a receptor. $\Delta G = \Delta H - T\Delta S$

Term	Description
<b>Enzyme</b>	A biological macromolecule, usually a protein (or less commonly an RNA molecule) which catalyses a specific reaction. They are often the target of drug action, particularly by inhibition
<b>Epidermal Growth Factor (EGFR)</b>	A cell surface receptor for factors that stimulate cell growth, proliferation and differentiation and whose overexpression is seen in a number of cancers and inflammatory conditions.
<b>Epidural injection</b>	The injection of analgesic / anaesthetic drugs into the space in the spine to enable medical procedures to take place in the lower body. It is an alternative to total anaesthesia
<b>Epigenetics</b>	Modifications to DNA or the proteins surrounding DNA in the nucleus which affect the ways that genes are turned on or off. This leads to differences between parent and child but because the genes causing the changes are not altered these are not heritable. Common modifications include covalent methylation of the DNA or proteins
<b>Epithelial cells</b>	Cells which line cavities and surfaces of blood vessels and organs throughout the body and exist in three principal shapes, squamous, columnar and cuboidal.
<b>Epitope</b>	A small section of an antigen that binds selectively to an antibody
<b>Equilibrium constant (K<sub>c</sub>)</b>	The ratio of the concentrations of the products of a reaction divided by those of the reactants at equilibrium. $A+B=C+D$ $K_c = \frac{[C][D]}{[A][B]}$
<b>Eudysmic ratio</b>	The ratio of the activity of the eutomer / distomer in the assay of interest, calculated using the respective EC <sub>50</sub> or IC <sub>50</sub> values. $ER = \frac{IC_{50}[\text{eutomer}]}{IC_{50}[\text{distomer}]}$

<b>Term</b>	<b>Description</b>
<b>Eukaryotes</b>	Organisms whose cells contain a nucleus and other organelles enclosed within membranes.
<b>European Agency for the Evaluation of Medicinal Products (EAEMA)</b>	The regulatory authority established under European Jurisdiction to authorise, control, and supervise the development and use of medicinal products.
<b>Eutomer</b>	The pharmacologically more active enantiomer of a chiral compound
<b>Excipient</b>	An additive in a drug formulation to aid dispersion, dissolution etc. of the active drug product.
<b>Excitatory neurotransmitter</b>	A neurotransmitter, e.g. glutamic acid, which on binding to the post-synaptic receptor causes a depolarisation of the neuron resulting in its excitation.
<b>Exclusion Criteria</b>	Characteristics which exclude a volunteer or patient from taking part in a specific clinical trial.
<b>Excretion</b>	The process whereby materials including drugs and constituents of food are removed from the body usually in urine and faeces.
<b>Exogenous factors</b>	Chemicals in the body which are not normally produced by the body

<b>Term</b>	<b>Description</b>
<b>Exposure</b>	The level of compound / drug observed in the body or a selected tissue after dosing
<b>Extracellular fluid</b>	All the body fluids found outside the cells, for example that found in blood, lymph, cavities, channels in the brain, spinal cord, in muscle and other tissues.
<b>Extravascular dosing</b>	Dosing by routes other than intravenously. (e.g. oral)
<b>False negative</b>	A compound which (usually based on existing SAR) would be expected to be active in an assay, but is inactive. May occur due to problems or errors with the assay or readout
<b>False positive</b>	A compound which initially appears to be active in an assay, but which on retest is inactive. Often occurs due to impurities in the sample, chemical degradation, aggregation or interference with the assay readout
<b>False substrate</b>	A drug which acts as a competitive substrate for an enzyme within a biochemical pathway thus disrupting its normal function.
<b>Fc Receptor</b>	A receptor on a cell surface which binds the unchanged / constant (Fc) region of an immunoglobulin and elicits an immune response
<b>Federal Drug Administration (FDA)</b>	A U.S. government agency charged with the regulation and approval of medicinal products

Term	Description
<b>Finished Product</b>	A product manufactured according to correct procedures which complies analytically with the established specification and has been released for use in clinical trials
<b>First pass effect</b>	The effect of drug metabolism in the liver after p.o. delivery. This is the first time that drug passes from the portal vein into the liver after dosing. Therefore this is often the highest drug concentration seen by the liver, thus the effect is at a maximum. The effect is much less of an issue for i.v., i.m. or s.c. delivery.
<b>First-in-Human Clinical Trials (FIH)</b>	Clinical trials exposing humans to a new chemical entity for the first time
<b>Foetus</b>	The development stage of a (for human) fertilised egg from around the 12th week of pregnancy to the birth of the baby.
<b>Follow-on</b>	A next generation clinical stage molecule, usually coming from the same originator company / organisation, and typically structurally distinct from the preceding drug. A follow-on compound introduces improvements to other aspects of the drug profile, such as better pre-clinical efficacy, selectivity or ADME.
<b>Formulation</b>	The physical drug form comprising the active pharmaceutical ingredient (API) and other required excipients which is dosed to patients
<b>Formulation Science</b>	The study of optimisation of the delivery of the active principal ingredient to patients
<b>Fragment</b>	A small molecule (~250Da or less) which binds weakly to a target and can be modified or combined with other fragments to enhance the binding affinity

Term	Description
<b>Fragment based drug discovery (FBDD)</b>	Drug discovery projects initiated using small molecular weight compound fragments in combination with an appropriate screening/assay system.
<b>Free binding energy</b>	The energy released when a ligand binds to its receptor. The stronger the binding the greater the free energy released.
<b>Full agonist</b>	A ligand which following binding, is capable of producing a 100% response in the target tissue, relative to the endogenous ligand
<b>G Protein</b>	An intracellular protein complex formed from different protein subunits, which bind guanine nucleotides and which are involved in cell signalling.
<b>G protein coupled receptors</b>	A class of receptors with seven transmembranal regions whose intracellular domain interacts with G proteins and which on activation by agonist binding initiates a cell signalling process.
<b>Gamma aminobutyric acid (GABA)</b>	An amino acid which is not normally used in protein synthesis, but is a major excitatory amino acid in the human nervous system.
<b>Gene</b>	A section of DNA responsible for coding for a specific protein.
<b>Gene expression</b>	The process whereby the information encoded in a section of DNA is converted to a protein.

Term	Description
<b>Gene silencing</b>	The technique of preventing genes from expressing their proteins, thereby providing information concerning its role in cell function. This can occur both in the transcription and the translation phases.
<b>Gene transcription</b>	See 'DNA transcription'
<b>Generic medicine</b>	A medicine which is biologically and chemically identical to a previously patented drug, but for which the patent has expired. Generic drugs are generally far cheaper than the branded equivalent.
<b>Genetics</b>	The science of genes and heredity.
<b>Genotoxin</b>	A molecule that causes damage to the genetic material of the cell.
<b>Genotype</b>	The organism's complete DNA sequence which comprises all of its genes.
<b>Gibbs Free Energy (G)</b>	The free energy of a system, the change in which following binding of a ligand to its receptor is denoted as $\Delta G$ .
<b>Glomerulus</b>	A network of capillaries in the kidney that perform the first step of filtering the blood at the beginning of the nephron.

Term	Description
<b>Glucagon</b>	A protein produced by the alpha cells of the pancreas, the action of which raises the concentration of glucose in the blood
<b>Glucuronidation</b>	The addition of glucuronic acid to a drug or its metabolites, usually in the liver, to greatly increase its water solubility and thus ease its excretion, particularly in the urine.
<b>Glucuronide</b>	A substance produced by the addition of glucuronic acid, an acid derived from glucose, to the drug or its metabolites. It is a key agent in the production of water soluble metabolites of xenobiotics which can be more easily excreted from the body.
<b>Glutamate</b>	A key intermediate in cellular metabolism and the most abundant excitatory neurotransmitter in the nervous system of vertebrates.
<b>Glutathione</b>	A tripeptide consisting of glutamate, cysteine and glycine which functions as an important <i>in vivo</i> antioxidant
<b>Glycoprotein</b>	Proteins which have carbohydrates attached to the amino acid chain.
<b>Good Clinical Practice (GCP)</b>	An established quality system to ensure that the planning, execution and reporting of clinical trials is carried out according to pre-agreed protocols, and that any deviations are recorded and justified.
<b>Good Laboratory Practice (GLP)</b>	An established quality system to ensure that the planning, execution and reporting of laboratory procedures is carried out according to pre-agreed protocols, and that any deviations are recorded and justified.

Term	Description
<b>Good Manufacturing Practice (GMP)</b>	An established quality system to ensure that the planning, execution and reporting of manufacturing processes is carried out according to pre-agreed protocols, and that any deviations are recorded and justified.
<b>Grb2 phosphorylation</b>	Growth factor receptor-bound protein 2 plays a key role in signal transduction initiated by growth factors. On phosphorylation it down-regulates tyrosine kinase signalling
<b>growth factor</b>	Proteinaceous and circulating signalling molecules which on binding to specific receptors stimulate cellular growth, proliferation and differentiation.
<b>Growth Inhibitory concentration (GI50)</b>	The concentration of a drug (usually an anti-proliferative) which reduces the growth of a tumour cell line by 50%. The test method follows an established protocol introduced by the National Cancer Institute (NCI)
<b>Half-life</b>	The time taken for the concentration of the drug to fall by 50% from the original value in the system under study
<b>Half-maximal inhibitory concentration (IC<sub>50</sub>)</b>	The concentration of compound required to inhibit the maximal biological effect in a specific assay by 50%. This term is <u>not</u> interchangeable with $k_i$ .
<b>Halogen bonding</b>	Non-covalent bonding between a halogen atom acting as an electrophilic species, and a Lewis base.
<b>Hapten</b>	A small molecule which can only elicit an immune response when attached to a much larger molecule, usually a protein.

Term	Description
<b>Heavy atom count</b>	The number of non-hydrogen atoms in a chemical structure. Often used to calculate Ligand Efficiency (LE) of a molecule.
<b>Henderson-Hasselbach equation</b>	An equation which relates the pH of a solution of an acid to its equilibrium constant (pka) and the log of the ratio of the concentrations of the protonated form to the ionised form. $\text{pH} = \text{pK}_a - \log_{10}([\text{A}^-]/[\text{HA}])$
<b>Heredity</b>	The passing of physical or mental characteristics from one generation to the next by genetic means.
<b>Heterodimeric protein</b>	A protein comprised of two distinct domains (or chains), each of which has a unique and different structure.
<b>High Throughput Screening (HTS)</b>	Biological assays carried out in parallel with automated plate handling, reagent addition and readout. Can be applied to recombinant isolated enzymes or whole cells (phenotypic screening). Typically involves testing tens to hundreds of thousands of compounds, usually in high density multiwell MTP formats.
<b>Higher Risk Agent</b>	An agent intended for medicinal use which despite benefits carries a greater risk of adverse events
<b>Hill Langmuir equation</b>	An equation generated by applying the law of mass action to the binding of an agonist to its receptor. $[\text{AR}] = ([\text{R}] \cdot \text{t} \cdot [\text{A}]) / ([\text{A}] + k_d)$
<b>Histones</b>	The highly alkaline proteins found in eukaryotic cell nuclei closely associated with DNA which they organise into structural units known as nucleosomes.

<b>Term</b>	<b>Description</b>
<b>Hit</b>	A compound which shows activity against the desired target when tested in a suitable assay, and which has had its structure confirmed
<b>Hit Confirmation</b>	The process during which the purity, structure and activity of the hit compound are firmly established.
<b>Hit Identification</b>	The process by which a series of molecules are assayed to establish those which give positive results, usually compared to a bench mark, in the chosen assay procedure
<b>Hit-to-Lead (HTL)</b>	The iterative modification of a hit molecule in order to maintain or improve its potency in the original assay, to assess the effects in other relevant assays and to start to build into it properties which are more likely to be useful as a drug when administered by the chosen route.
<b>Homeostasis</b>	The process whereby the organism keeps a constant internal environment, e.g. the body temperature.
<b>Homodimer</b>	A macromolecular complex formed from two identical unit of, e.g. receptors, proteins or nucleic acids.
<b>Homodimeric protein</b>	A protein comprised of two distinct domains (or chains), each of which has the same structures.
<b>Hormone</b>	Signalling molecules produced by glands in multicellular organism which enter the circulatory system and are carried to the target tissues. Examples include adrenaline, steroids, growth hormones and peptides such as oxytocin

Term	Description
<b>Human ether-a-go-go related gene (hERG)</b>	The gene which codes for a protein sub-unit of the Kv 11.1 potassium channel in heart muscle tissue, and disruption of which can cause QT prolongation. Interaction with the hERG protein is frequently used to assess the potential of novel agents to have potential cardiotoxic liabilities.
<b>Hydrogen Bond Acceptor (HBA)</b>	Heteroatom or group, e.g. C=O, which binds to a hydrogen bond donor motif in an intramolecular interaction. It is important for drug affinity.
<b>Hydrogen Bond Donor (HBD)</b>	Hydrogen containing group such as OH, NH or SH which binds to a hydrogen bond acceptor motif in an intramolecular interaction.
<b>Hydrogen Bonding</b>	An electrostatic interaction between the hydrogen atom of O-H, N-H and S-H units and electronegative atoms or groups such as O and carbonyls. This is responsible for a significant proportion of a drug-receptor interaction.
<b>Hydrophilic</b>	A term used to describe a molecule which is more soluble in aqueous solution than in lipid media.
<b>Hydrophobic</b>	A term used to describe a molecule which is more soluble in lipid or fatty solvents than it is in aqueous solution.
<b>Hyper polarisation</b>	A change in the membrane potential of a cell which makes it more negative. This is usually caused by efflux of potassium cations or the influx of chloride anions.
<b>Idiosyncratic effect</b>	An effect which is unpredictable, and seems to be restricted to a very small number of individuals.

Term	Description
<b>Idiosyncratic toxicology</b>	A unanticipated toxic effect of a drug which appears to be restricted to a very small number of people.
<b>Immune response</b>	The response of the body's immune system to the appearance of a foreign protein or pathogen in the bloodstream.
<b>Immune system</b>	A highly complex defensive system in the body whose function is to protect it from invasion by pathogens, particularly viruses, parasitic worms and proteins different from the body's own. It is classified into different subsystems including the innate and adaptive immune systems, the humoral system and the cell-based system.
<b>Immunity</b>	The ability of a body to resist invasion by specific pathogens, such as viruses. Immunity is usually the result of prior exposure to the virus or to a modified (or inactive) form of the virus given deliberately in inoculations.
<b>Immunoglobulins</b>	Glycoproteins produced by white blood cells that bind to antigens and thus aid their destruction as part of the immune response. They can be found as both soluble and membrane-bound entities.
<b>In silico</b>	Computer simulations which model likely behaviour of properties of a molecule in a biological system, for example binding to an enzyme or receptor
<b>In vitro</b>	An experimental procedure involving the use of isolated tissue, cells or enzymes i.e. a non-whole animal system. Usually will be carried out in test tubes, vials, culture dishes, MTPs or other similar vessels.
<b>In vivo</b>	Literally 'in life' (Latin); an experimental procedure carried out by dosing the compound in a whole animal. Typically this refers to pharmacokinetic, pharmacodynamic, efficacy or toxicology assessment.

Term	Description
<b>Infectious agent</b>	Agents including prions, viruses, bacteria, fungi, protozoa and worms that replicate inside the body of the host and cause disease.
<b>Infusion</b>	The dosing of a solution of drug (usually) into the veins over a period of time.
<b>Inhalation</b>	Dosing of drugs directly into lungs using aerosols or a device such as a spin inhaler.
<b>Inhibitor</b>	A molecule which prevents the interaction of receptor and enzymes with their ligands or co-factors
<b>Inhibitory rate constant (<math>K_i</math>)</b>	The kinetic constant which reflects the binding potency of an enzyme inhibitor (i.e. formation of the $EI^*$ complex). It differs from $IC_{50}$ in that it is independent of the concentration of endogenous co-factor used in the assay.
<b>Injection</b>	The dosing of solutions of drug as a single bolus into the body using a syringe and hypodermic needle.
<b>Institutional Animal Care and Use Committee (IACUC)</b>	Oversees an institution's animal care program and is responsible for reviewing all animal use protocols, ensuring compliance with federal regulations, inspecting animal facilities and laboratories, and overseeing training of animal handlers
<b>Insulin</b>	A peptide hormone produced by the $\beta$ -cells of the pancreas which promotes the absorption of glucose from the blood to skeletal muscle and fat tissue thus regulating the metabolism of fats and carbohydrates. Damage to the production of insulin leads to diabetes.

Term	Description
<b>Intellectual property (IP)</b>	In the context of drug research, this refers to information which can be protected (e.g. using patents or trademarks). This usually involves novel molecules, their therapeutic application and their preparation.
<b>Intercalation</b>	The insertion of molecules between the planar bases of DNA. It is a mode of action of a number of chemotherapeutic agents.
<b>Interstitial fluid</b>	A solution that bathes the tissue cells of multicellular animals including humans. In an adult this amounts to ca 10L of fluid and is essentially blood plasma without the plasma proteins.
<b>Intestinal epithelium</b>	The layer of columnar cells covering the inner face of the intestinal tract.
<b>Intra-arterial dosing (i.a.)</b>	Injection of a solution of drug directly into the arterial bloodstream
<b>Intracerebral dosing (i.c.)</b>	The injection of a solution of drug directly into the cerebrospinal fluid
<b>Intramuscular dosing (i.m.)</b>	The injection of a solution of drug into muscles.
<b>Intraperitoneal dosing (i.p.)</b>	The injection of a solution into the peritoneal cavity

Term	Description
<b>Intrathecal dosing</b>	Injection or infusion of a solution of drug into the spinal cord.
<b>Intravascular dosing</b>	Injection of a solution of drug directly into the bloodstream, usually via veins (intravenous) but on rarer occasions into arteries (intra-arterial)
<b>Intravenous dosing (i.v.)</b>	Injection of a solution of a drug into veins.
<b>Inverse Agonist</b>	An agent which binds to the same receptor binding site as an agonist for that receptor and reverses constitutive activity of the receptors. Inverse agonists can exert the opposite pharmacological effect of a receptor agonist
<b>Investigational Medicinal Product (IMP)</b>	An chemical substance whose clinical effects are to be studied
<b>Investigational New Drug (IND)</b>	A molecule which has been approved by the FDA for investigational use in human clinical trials.
<b>Investigational Review Board (IRB)</b>	Committee within an institution that has been formally designated to approve, monitor, and review biomedical and behavioural research involving humans
<b>Investigators Brochure</b>	A dossier prepared in order to record and communicate to the clinical principal investigator (PI) the established properties of the medicinal product and the protocol for the clinical investigations planned

Term	Description
<b>Ion channel</b>	A water-filled pore in the cell membrane formed by a proteinaceous lining through which ions, mainly hydrogen sodium, potassium and calcium pass into and out of the cell
<b>Ionisable groups</b>	Neutral groups which gain or lose protons in physiological media and thus become positively or negatively charged. This can affect permeability, and therefore absorption.
<b>Ionisation</b>	The loss or gain of a proton from acids and bases respectively.
<b>Ionisation constant (pKa)</b>	A measure of the strength of an acid which is numerically equal to the negative logarithm of the ionisation constant of the acid. It is also the pH of a solution at which the acid is 50% ionised. $pka = -\log_{10} K_a$
<b>Ionisation state</b>	The molecular state resulting from gain or loss of protons.
<b>Ionotropic effect</b>	A biological response which involves the movement of ions.
<b>Ionotropic receptor</b>	A receptor in which binding of an agonist induces the opening of an ion channel
<b>Isostere</b>	A structural motif which is atomically distinct from another, but forms similar interactions. Isosteres with the same biological properties are termed bioisosteres.

Term	Description
<b>Isothermal Titration Calorimetry (ITC)</b>	A physical chemical technique used to measure quantitatively the interaction between small molecules and biological macromolecules
<b>Isozyme</b>	Enzymes differing in amino acid sequence but which catalyse the same chemical reaction and are in the same sub-family. They usually display different kinetic parameters or regulatory properties to other family members.
<b>Kinase</b>	A large group of enzymes which transfer phosphate groups from high energy sources such as adenosine triphosphate (ATP) to nucleophilic groups such as hydroxyl, amino, thio on specific amino acids in substrate proteins. Examples include tyrosine and serine / threonine kinases
<b>Kinase cascade</b>	A series of kinase enzymes in which one enzyme initiates a signalling cascade by phosphorylating and activating the next enzyme, thus activating it which in turns activates another and so on.
<b>Kinase linked receptor</b>	A transmembranal protein in which the receptor region is found on the extracellular domain and there is kinase activity on the intracellular domain. Activation of the receptor induces kinase activity thus initiating the cellular response. Examples include epidermal growth factor receptor, vascular endothelial growth factor receptor etc.
<b>Kinetic solubility</b>	The non-equilibrium concentration of a substance dissolved in a solvent at a given time
<b>Large-scale synthesis</b>	The large scale manufacture of a material intended for clinical use by safe, reliable and reproducible means
<b>Lead</b>	A molecule with the targeted biological activity that then provides the basis for subsequent structure-activity investigations

Term	Description
<b>Lead Optimisation (LO)</b>	The chemical manipulation of the lead structure to maximise the desired biological activity, introducing drug-like properties, whilst minimising unwanted side effects
<b>Libraries (of compounds)</b>	Collections of large numbers of compounds of related structures which are often prepared using parallel synthesis methodologies, and are commonly used as a starting point for biological screening in drug discovery programmes
<b>Ligand</b>	A molecule which binds to a receptor or enzyme causing a biological effect. The definition includes both agonists, antagonists and inhibitors.
<b>Ligand Based Design</b>	A drug design strategy which uses an existing ligand for the target receptor as the lead structure.
<b>Ligand Efficiency (LE)</b>	A measure of the strength of binding of a ligand to its receptor or enzyme. More specifically it is the binding energy per atom of the ligand and is defined as the ratio of the Gibbs free energy ( $\Delta G$ ) to the number of non-hydrogen atoms (N) in the molecule. $LE = \Delta G / N$ or $1.4(pk_i / N)$
<b>Ligand efficiency dependent lipophilicity (LELP)</b>	A parameter defined as the lipophilicity of a molecule divided by its ligand efficiency. It is a metric often used to assess quality within a collection of hit molecules, with a value of between 0 and 7.5 for optimum activity. $\log P / LE$
<b>Ligand gated channel</b>	An ion channel which is can be controlled by binding of ligands to specific receptors on the proteins.
<b>Ligand-lipophilicity efficiency (LiPE)</b>	Also termed lipophilic efficiency (LiPE). A parameter which attempts to quantify the dependence of the binding potency of a compound to its lipophilicity, and thereby predict drug-likeness. It is defined as the difference between the activity ( $-\text{LogIC}_{50}$ ) and the $\log P$ . Best compounds have $\log IC_{50}$ values between 7 & 8 and $\log P$ between 0 and 3 giving LiPE of around 6. $LLE = pIC_{50} - \log P$

Term	Description
<b>Lineage</b>	The development history of a tissue from the fertilised embryo to the functioning organ detailing the intermediate cell lines involved.
<b>Lipids</b>	A group of hydrophobic or amphiphilic molecules including fats, sterols, monoglycerides, diglycerides, phospholipids and fatty acids
<b>Lipinski's Rules</b>	A set of rules which are often used to predict the likely oral availability or "drug-likeness" of new molecules, based on a retrospective 1998 analysis by Lipinski et al of currently available oral drugs. These are based on molecular weight (<500), numbers of hydrogen bond donors (<5) and acceptors (<10) and their oil/water coefficient of partitioning (<5).
<b>Lipophilic compounds</b>	Molecules which are more soluble in fatty, oily media rather than water
<b>Lipoproteins</b>	Biochemical assemblies that contain both proteins and lipids bound to the protein that allow fats to move through water both inside and outside the cell.
<b>Liver</b>	A large organ of the human body one of the functions of which is as the major site of metabolism of exogenous materials including food and drugs.
<b>Liver Microsomes (HLM, MLM, RLM)</b>	Subcellular fraction isolated from homogenised liver cells which contain the enzymes responsible for metabolising drugs. Often used for in vitro assessment of drug metabolic stability.
<b>Logarithm of distribution (LogD)</b>	A logarithmic expression of the distribution of a molecule between an organic phase, often octanol and water at variable pH and at which some of the molecules may be ionised. $\text{LogD}(\text{pH}) = \text{Log} [\text{organic phase}]/[\text{aqueous phase}]$

Term	Description
<b>Logarithm of partition (LogP)</b>	A logarithmic expression of the partition coefficient of a molecule between an organic phase, often octanol, and water at a pH where all the molecules are neutral. $\text{Log P} = \log[\text{organic phase}]/[\text{water phase}]$ at equilibrium.
<b>Lowest Effective Concentration (LEC)</b>	The lowest concentration in an assay that gives a positive signal. Often used in toxicological tests such as cytotoxicity
<b>Lumen</b>	The inner space of a tubular structure such as a blood vessel or the intestine
<b>Lymph</b>	A clear fluid which is generally similar to blood plasma but which contains white blood cells, and circulates via the lymphatic system
<b>Lymphatic system</b>	A network of vessels that carry lymph towards the heart and is part of the circulatory system along with the blood vessels. It plays a major role in the immune system.
<b>Lymphocytes</b>	White blood cells which are a major part of the body's immune process and are comprised of natural killer (NK) cells, T cells and B cells.
<b>Lysosomes</b>	Membrane bound organelles found in most animal cells which contain a variety of hydrolytic enzymes whose purpose is to remove unwanted macromolecules in the cell.
<b>Madin-Darby canine kidney membrane assay (MDCK)</b>	Epithelial cell line from canine kidneys which is used as a model membrane for in vitro permeability studies. This has only low expression of transporter proteins and low metabolic activity

Term	Description
<b>Matched Molecular Pair</b>	A technique used in chemoinformatics which describes pairs of molecules differing in only single point changes, and their associated potency. It is used in structure-activity work to study changes in biological activities in a series of molecules.
<b>Maximum plasma concentration (C<sub>max</sub>)</b>	The maximum concentration of a drug in the blood plasma reached after administration at a particular dose.
<b>Median effective dose (ED<sub>50</sub>)</b>	The dose producing a response that is 50 per cent of the maximum obtainable. ED50 values provide a useful way of comparing the potencies of drugs that produce physiologically similar effects at different concentration
<b>Mediator</b>	A generic term for endogenous substances released in the body that produce profound physiological effects. Representative examples include bradykinin, platelet activating factor, prostaglandins and nitric oxide. They represent targets for pharmacological action in a number of disease states.
<b>Medicinal chemistry</b>	The science of chemistry targeted towards discovering, designing and optimising biologically active molecules with the potential for therapeutic benefit in human diseases
<b>Medicine</b>	A preparation which when administered to a human organism is intended to produce a beneficial effect.
<b>Medicines and Healthcare Products Regulatory Agency (MHRA)</b>	A UK government agency responsible for regulating the use of all medicines and medical devices.
<b>Meiosis</b>	A cell division process in which the existing genetic material is split, and gametes (sperm or eggs) are produced, with each new cell comprising only 23 single chromosomes. Subsequent fertilisation restores the 23 pairs of chromosomes to the cells of the embryo.

Term	Description
<b>Membrane</b>	A barrier enclosing a cell or tissue, largely comprised of phospholipids in which are found a range of proteins such as transporters and ion channels which are essential for the functioning of the cell.
<b>Metabolic blocking</b>	The inhibition of a drug's metabolic pathway due either to a genetic effect or the presence of an inhibitor of the enzyme such as a co-administered drug. This can lead to extended time of action of the initial drug.
<b>Metabolic enzymes</b>	Enzymes which act on drugs to modify their structure thus facilitating their elimination from the body. They are usually oxidative enzymes although reductases and hydrolases are also present.
<b>Metabolism</b>	In the context of drug discovery, the way in which the body deals with exogenous materials such as drugs
<b>Metabolite</b>	A product resulting from the enzymatic modification of a molecule after exposure to metabolising enzymes either in vivo, after administration or in vitro after exposure to isolated enzymes or liver extracts.
<b>Metabolome</b>	The total collection of metabolites produced in any given cell, tissue or organism. It can also refer to all the metabolites of a xenobiotic.
<b>Metabotropic glutamate receptor</b>	A type of glutamate receptor which is not an ion channel. They consist of seven transmembranal domains, and are found widely in the central and peripheral nervous system. They are believed to be involved in learning, anxiety, memory and the perception of pain.
<b>Metabotropic receptor</b>	A subset of neurotransmitter receptors which are indirectly linked to ion channels in plasma membranes by secondary messengers such as G-proteins.

Term	Description
<b>Me-too compound</b>	A semi-colloquial term used most often by those outside of the drug discovery industry to describe superficially similar compounds within the same therapeutic class.
<b>Microdose</b>	An extremely low (sub-therapeutic) dose, often radiolabelled, of a medicinal product which can be administered to a volunteer or a patient in a phase zero or early phase one clinical trial
<b>Microsomal triglyceride transfer protein (MTTP)</b>	A heterodimeric protein that plays a central role in lipoprotein assembly.
<b>Microtitre plate</b>	A (usually) plastic plate containing 96, 384 or 1636 wells used for conducting biological assays.
<b>Mitochondria</b>	The subcellular organelles which are responsible for energy generation
<b>Mitogen</b>	A protein or biomolecule which causes the process of cell division to start
<b>Mitogen activated protein kinase (MAPK)</b>	Phosphate transfer enzymes whose action is specific to serine, threonine and tyrosine. They are involved in cell signalling responses to mitogens, osmotic stress, heat shock and proinflammatory cytokines and regulate cell functions such as proliferation, gene expression, differentiation, mitosis and apoptosis.
<b>Mitosis</b>	A cell division process in which the existing genetic material is duplicated, and two new cells identical to the parent cell are produced. In this process the chromosomes are copied exactly.

Term	Description
<b>Molecular biology</b>	The scientific discipline which seeks to understand biology at the molecular level
<b>Monoclonal Antibody</b>	An antibody raised in animals (usually rabbits) to a specific peptidic antigen and comprising a single antigenic structure. Can be for use as a medicinal product or biological reagent
<b>Monooxygenase</b>	The main class of enzymes used in mammals to metabolise drugs by adding one hydroxyl group. Examples include the cytochrome P450s
<b>Mutagenicity</b>	The ability of a physical or chemical agent to modify a cells genetic material, potentially leading to the formation of cancerous cells.
<b>National Institute for Health and Care Excellence (NICE)</b>	A UK government body which sets guidelines for the use of drugs, and other medical procedures, in the most efficient way possible.
<b>N-dealkylation</b>	A major route of metabolism in which an alkyl group attached to an amino group is first oxidised to an aminal, which subsequently cleaves to produce the parent amine with an aldehyde by-product
<b>Nephron</b>	The basic structural unit of the kidney which eliminates waste products and regulates blood volume and pressure.
<b>Nerve terminals</b>	The distal end of a nerve cell where it either meets another nerve cell, or its target muscle. At the terminal a neurotransmitter is released into the synaptic cleft, thereby maintaining the electric impulse.

Term	Description
<b>Nervous system</b>	The system formed from nerve cells (neurons) which control all the thought processes of the body, all the conscious movements of the body and the involuntary movements such as breathing, heart beating etc.
<b>Neuron</b>	The cells forming the nervous system. Many have characteristic shapes of long cell bodies with numerous points of interaction with other neurons or muscle cells to perform their functions. Some neurons, e.g. the sciatic nerve, which stretches the whole length of the leg are extremely large.
<b>Neurotransmitter</b>	An endogenous chemical, which following an electric impulse is released into the synaptic cleft. On arrival at receptors of target neurones (nerve cells) it reinitiates the electric impulse thereby maintaining the transmission of an electrical potential from one neurone to another.
<b>New Chemical Entities (NCEs)</b>	Novel small molecules whose structure and chemical, and, in the context of drug discovery, biological properties have not been previously described
<b>Nicotinamide adenine dinucleotide (hydride) (NAD(H))</b>	An important cofactor for widely distributed redox enzymes which catalyse the reduction of substrates in mammalian cells.
<b>No Observed Adverse Event Level (NOAEL)</b>	The highest dose level given to the volunteer or patient which does not result in the observation of an adverse event attributable to the drug
<b>Non-competitive antagonism</b>	A compound that decreases receptor activity by binding at an allosteric site; this being a site which does not bind the endogenous agonist. Changes in endogenous agonist concentration will not overcome this.
<b>Non-Competitive Inhibitor</b>	A compound that inhibits an enzyme by binding at an allosteric site, this being one which does not bind the endogenous substrate. Changes in endogenous substrate concentration will not overcome this type of inhibition.

Term	Description
<b>Nuclear Medicine</b>	The therapeutic or diagnostic use of substances which are enriched with nuclei other than the natural isotopes. Most commonly this uses radioactive materials such as $^{18}\text{F}$ but can include stable isotopes such as $^{13}\text{C}$ .
<b>Nuclear receptors</b>	A group of proteins found within the nucleus of the cell which bind steroid and thyroid hormones and initiate expression of specific genes thus controlling the development, homeostasis and metabolism of the organism. They can also act as receptors for a range of drugs.
<b>Nucleic acid</b>	A large biopolymer formed, in the case of DNA, from chains of the purines (adenosine or guanine), and pyrimidines (cytosine and thymine), each carrying the sugar deoxyribose and a phosphate group. In the case of RNA the pyrimidine uracil replaces thiamine and the sugar is ribose. The biopolymer comprises many thousands of bases usually as a helix of two chains running in opposite directions.
<b>Nucleosome</b>	A macromolecular complex of DNA wound around eight histone protein cores which makes up the basic unit of DNA packaging in eukaryotes.
<b>Nucleus</b>	A cellular organelle surrounded by a membrane in which is found most of the cells genetic material and its associated proteins.
<b>Occupancy</b>	The amount of drug bound to the active site of a receptor. In the receptor occupancy model of drug action, the magnitude of the drug response is directly proportional to the amount of the drug bound to the receptor.
<b>Off-label</b>	The use of a drug in a manner different to that which was specifically approved by the regulatory authorities.
<b>Off-target</b>	The interaction of a drug with enzymes or receptors other than those for which it was designed. Such interactions are often, but not always associated with toxicity or other adverse effects.

<b>Term</b>	<b>Description</b>
<b>Oncogene</b>	A gene that if activated has the potential to produce proteins that can cause cancer.
<b>Oncology</b>	The medical discipline directed towards the treatment of cancers
<b>Onco-protein</b>	A protein produced by an oncogene.
<b>Open label (clinical trial)</b>	A clinical trial in which patients are aware that they are being dosed by a physician with a candidate drug
<b>Organelle</b>	A subunit within a cell that has a defined, specialised function
<b>Organic cation transporters</b>	A family of proteins that mediate the transport of organic cations and zwitterions across the cell membrane. A related family transport organic anions.
<b>Orthosteric inhibitor</b>	A compound which binds to the same active site in an enzyme as the endogenous substrate
<b>Osmosis</b>	The movement of water from an area of low solute concentration through a semi-permeable membrane to an area of high solute concentration

Term	Description
<b>Oxidases</b>	A class of enzymes which raise the oxidation level of the substrate by the addition of hydroxyl groups, oxygen atoms or by dehydrogenation.
<b>Pancreas</b>	The organ in the body responsible for producing the enzymes required for the digestion of food, as well as the hormone insulin which controls blood glucose levels.
<b>Paracellular</b>	The transport of materials through a membrane via the water-filled intercellular spaces rather than through the cells themselves. An example is the reabsorption of sodium ions in the proximal tubule of the kidney nephrons
<b>Parallel artificial membrane permeability assay (PAMPA)</b>	An artificial membrane formed from hexadecane in hexane which is used to measure passive diffusion of compounds <i>in vitro</i>
<b>Parasympathetic nervous system</b>	The part of the involuntary nervous system responsible for slowing the heart rate and stimulating a so-called "rest-and-digest" mode following eating. It is complementary to the sympathetic nervous system.
<b>Partial agonist</b>	A compound which acts on a receptor to give less than a maximal response even at high concentrations.
<b>Partition coefficient</b>	The ratio of the concentrations of a compound in two non-miscible layers. In drug research, the layers are usually water and n-octanol and the partition coefficient is often used as a surrogate for membrane permeability
<b>Passive transport</b>	The movement of molecules through a biological membrane along a concentration gradient and not via interaction with specific carriers for the compound.

<b>Term</b>	<b>Description</b>
<b>Patent</b>	A legal and scientific document describing and preventing the exploitation of a commercially useful invention by other than the named inventors for a defined time period
<b>Pathogens</b>	Microorganisms such as bacteria, viruses and prions that cause disease.
<b>Peptidase</b>	Enzymes responsible for the hydrolysis of peptides.
<b>Peptide</b>	A chain of amino acids linked through amide bonds distinguished from proteins by having less than 50 amino acids.
<b>Percentage ionised</b>	A measure of the amount of acid or base existing in an ionised form in a particular physiological situation.
<b>Percutaneous administration</b>	A dosage regimen in which the drug passes through the skin into the circulation following topical application, or by sustained release from patches fixed to the skin.
<b>Parenteral dosage</b>	A dosage regimen in which the drug is introduced into the body through any route other than via the digestive tract.
<b>Peripheral nervous system</b>	The part of the nervous system outside of the brain and spinal cord.

Term	Description
<b>Permeability (compound)</b>	The ability of a compound to penetrate a cell wall or biological membrane. Common in vitro systems used to assess this are caco-2, MDCK and PAMPA
<b>Permeability (membrane)</b>	The susceptibility of a biological membrane to penetration by exogenous chemicals
<b>Permeability coefficient</b>	A compound specific physical parameter which quantifies its ability to cross biological membranes. The magnitude depends on factors such as molecular size, lipid solubility and active efflux
<b>P-glycoprotein (P-gp or Pgp)</b>	A 170kDa transmembrane protein whose expression is both ubiquitous and inducible, and whose function is to pump foreign substances, including drugs, out of cells. It is particularly important in the blood-brain barrier and some cancer cells which express such large amounts that this complicates anti-cancer drug treatments. Also known as multidrug resistant protein 1 (MDR1) or ATP-binding cassette sub-family B member 1 (ABCB1) or cluster of differentiation 243 (CD243)
<b>Pharmacodynamics</b>	The study of the variation with time of the effects of an administered substance on the body
<b>Pharmacokinetic antagonism</b>	The situation in which one drug effectively alters the concentration of another at its site of action. This can be by altering the rate of absorption of the drug or the rate of its metabolism. This is potentially very important in patients who are taking more than one drug.
<b>Pharmacokinetic-pharmacodynamic relationship (PK-PD)</b>	A technique that combines the study of pharmacokinetics (PK) with pharmacodynamics (PD) thus giving a full profile of the time course of exposure and action of the drug. A PK-PD relationship attempts to explain the PD effects of a drug in relation to the amounts present.
<b>Pharmacokinetics</b>	The study of the variation with time of the concentration of a molecule or its metabolite(s), usually but not uniquely in the plasma, following administration

Term	Description
<b>Pharmacological Probe</b>	A compound used as a biological tool substance, which has potent biological activity but is not a clinically useful drug
<b>Pharmacology</b>	The study of the effect of chemicals or drugs on living organisms such as animals and humans.
<b>Pharmacopoeia</b>	A reference volume or online database containing information on the therapeutic action of all drugs available to the physician.
<b>Pharmacovigilance</b>	Exercising the discipline of collecting information concerning the effects of an administered substance, particularly with regards to adverse effects.
<b>Phase 0 clinical trial</b>	Clinical studies carried out at a sub-therapeutic micro-dose to establish the pharmacokinetic and pharmacodynamic properties of the administered substance in a very small number of healthy volunteers
<b>Phase 1 clinical trial</b>	Clinical studies carried out in volunteers and in some cases patients (e.g. for cancer) to determine the pharmacokinetic and tolerance levels of an administered drug
<b>Phase 1 metabolism</b>	The initial (usually) oxidative phase of metabolism of drug molecules in which polar functionalities such as hydroxyl, thiol or amino are introduced to aid elimination. These can subsequently be conjugated to highly water soluble entities such as glucuronic acid in Phase 2 metabolism.
<b>Phase 2 clinical trial</b>	Clinical studies carried out in patients to establish the efficacy of the administered substance. These are often divided into either Phase 2a (exploratory, proof-of-concept) or Phase 2b (definitive). At the end of Phase 2 a defined dosing regimen will have been established for pivotal registration trials. Trials are often carried out compared to placebo.

Term	Description
<b>Phase 2 metabolism</b>	The conjugative phase of drug metabolism in which highly water-soluble groups such as glucuronic acid, glycine and glutathione are added to the drug or metabolite to enable them to be eliminated from the body.
<b>Phase 3 clinical trial</b>	Pivotal, registration enabling clinical studies carried out in order to confirm the efficacy of the administered substance in a statistically significant manner, using a wider and representative patient population with the dosing regimen defined in Phase 2. May be carried in comparison to placebo control or current standard-of-care.
<b>Phase 4 clinical trial</b>	Post-registration studies carried out to compare the administered substance with current therapies to facilitate prescribing recommendations and policies
<b>Phenotype</b>	The observable characteristic of an organism which result from a specific genotype
<b>Phenotypic assay (screening)</b>	An assay system which measures the effect of the candidate compounds on the phenotype of the target organism
<b>Phospholipidosis</b>	A disorder characterised by excessive accumulation of phospholipids in tissues. It is a common side effect of a number of drugs particularly cationic amphiphilic molecules
<b>Phosphatase</b>	An enzyme that catalyses the removal of a phosphate group from a phospho-hydroxyl group on serine, threonine or tyrosine residues in proteins.
<b>Phospholipases</b>	Enzymes that catalyse the hydrolysis of phospholipids either at one of the ester groups to release a fatty acid (phospholipases A1 and A2) or at the hydroxyl group bearing a phosphate group to release the phosphate (phospholipase C).

Term	Description
<b>Phospholipids</b>	A class of naturally occurring molecules the backbone of which is a glycerol molecule. Two of the hydroxyl groups are esterified by long-chain fatty acids, with the third carrying a phosphate or phosphatylcholine group. They are essential elements of cell membranes.
<b>Physiological antagonism</b>	The behaviour of a substance that produces effects countering those of other substances, not necessarily involving binding to the same receptors.
<b>Pinocytosis</b>	A non-selective process whereby a cell engulfs a small quantity of extracellular fluid, thus forming an invagination of the cell surface. Fusion of the cell membranes thus forms a vesicle inside the cell, with the contents being broken down following processing by lysosomes.
<b>Placebo</b>	A dosing formulation which is apparently identical to the drug but which contains no active pharmaceutical ingredient
<b>Plasma</b>	The pale yellow liquid component of blood which holds the blood cells in suspension.
<b>Plasma concentration</b>	The concentration of a drug in the plasma at a particular time point
<b>Poison</b>	A substance which when administered to a living organism produces a deleterious effect
<b>Polar surface area (PSA; TPSA)</b>	The molecular surface area summed in Å <sup>2</sup> over all the polar atoms of a drug, primarily oxygen and nitrogen (sometimes sulfur) and their associated hydrogen atoms. It is a metric often used during the optimisation of a drug's ability to permeate cells.

Term	Description
<b>Poly pharmacology</b>	An approach to the treatment of disease by using either a combination of drugs affecting more than one receptor or a drug which itself reacts with more than one receptor. It is likely that this will be more efficient for diseases which affect a number of organs or tissues.
<b>Polyclonal antibodies</b>	Antibodies produced by a range of B cells in response to an antigen and which recognise multiple epitopes on that antigen
<b>Polymerase chain reaction (PCR)</b>	A biochemical method used to amplify samples of nucleic acids by use of polymerase enzymes and excess amounts of all four nucleosides.
<b>Polymorph</b>	A different crystal form of the same compound. These are important in solid drug substances because alternative polymorphs can have different solubilities, and thus different absorption properties and different clinical profiles
<b>Polymorphism</b>	The ability of a solid to exist in different forms or crystal structures.
<b>Portal system</b>	A system of blood vessels associated with the liver and consisting of the portal vein and its tributaries. It directs blood from the gastrointestinal tract to the liver so exposes drugs absorbed from the GI tract to the metabolising enzymes found there
<b>Post synaptic membrane</b>	The membrane in the synapse containing the receptor for neurotransmitters.
<b>Post-marketing surveillance</b>	The process whereby a drug newly released into the general population is monitored to ensure that there are no significant rare side-effects that were not detected in the much smaller patient numbers used in clinical trials

Term	Description
<b>Potency</b>	The potency of a drug is determined by the dose needed to give a desired effect. Thus the smaller the dose, the greater the potency. Often used in a quantitative sense to compare between different drugs.
<b>Pre-Clinical Studies</b>	Studies undertaken before and during clinical trials to ensure as far as reasonably possible the safety of the substance to be administered to humans and to facilitate the choice of the dose levels required in order to observe beneficial effects. Usually involves a selection of <i>in vitro</i> and animal toxicology and efficacy studies.
<b>Pre-systemic metabolism</b>	Drug metabolism that occurs in the gut before absorption into the circulation, often as a result of the gut flora and gut wall enzymes
<b>Principal Investigator (PI)</b>	The lead clinician responsible for conducting the clinical studies of a new medicinal product at a particular trial centre
<b>Prion</b>	The smallest known proteinaceous disease-causing infectious agent. They consist of misfolded proteins, and do not seem to contain genetic material. They are believed to cause a number of degenerative conditions including mad cow disease, kuru and Creutzfeldt-Jacob disease.
<b>Privileged (structure or scaffold)</b>	A structural class has often been found to be active against particular biological targets, or in specific therapeutic indications.
<b>Pro-drugs</b>	An administered agent which is converted in the body into the active drug substance. This can be due to enzymatic action (e.g. enalapril) or to changes in acidity in the GI tract (e.g. losec)
<b>Prokaryote</b>	Single cell organisms that lack a membrane bound nucleus or other organelles. They can be subdivided into bacteria and archaea.

Term	Description
<b>Proliferation</b>	The process whereby cells divide, grow and expand their population
<b>Proof of Concept</b>	Usually the <i>in vivo</i> demonstration that the underlying project hypothesis is valid, for example that modulation of a specific target enzyme or biological pathway has a beneficial effect on a disease or phenotype
<b>Prostaglandins</b>	A class of physiologically active lipid molecules derived from arachidonic acid which mediate a range of hormonal activities including pain, fever, inflammation, platelet aggregation and effects on vascular smooth muscle cells.
<b>Protein</b>	A chain of amino acids linked through amide bonds distinguished from peptides by having more than around 50 amino acids.
<b>Protein binding</b>	The process whereby small molecules or ions complex non-covalently and non selectively to proteins such as albumin or alpha-1-acid glycoprotein (AGP or a1AGp or AAG)
<b>Protein Data Bank</b>	A web resource which serves as a repository for protein / ligand crystal structures. Data can be downloaded and manipulated locally
<b>Protein synthesis</b>	The synthesis of protein from the constituent amino acids on the ribosome
<b>Protein-protein interactions</b>	Two or more proteins interacting via specific regions on their surface. This results in conformational changes and further reactions, and is particularly important for a wide range of biochemical processes such as cell signalling.

Term	Description
<b>Proteomics</b>	The science of understanding the total collection of proteins expressed by a cell or organism under a given set of conditions.
<b>Proteosome</b>	A complex structure inside all eukaryotic cells whose function is to degrade unwanted or damaged proteins.
<b>Protocol</b>	In the context of clinical trials, the agreed procedures to be followed by all investigators and is documented in the investigators booklet.
<b>Proto-oncogene</b>	A normal gene that becomes an oncogene through mutation or increased expression. For example, c-Src
<b>Protozoa</b>	A diverse group of unicellular eukaryotes including amoeba which are the cause of a number of human diseases including malaria, dysentery and sleeping sickness.
<b>Q wave</b>	A downward deflection in the electrocardiogram which represents depolarisation of the interventricular septum, the stout wall which separates the lower chambers of the heart.
<b>QT Interval (QT)</b>	A measurement of the time gap between the Q and T points on an electrocardiogram, variation from the standard can indicate the possibility of cardiac toxicity and serious adverse events. A number of drugs are known to affect QT interval, and therefore care needs to be exercised in their use.
<b>Qualified Person (QP)</b>	A designated person with sufficient training, knowledge and experience to approve studies supporting clinical investigations

<b>Term</b>	<b>Description</b>
<b>Quality Assurance (QA)</b>	The verification of procedures to be used and the recording of the processes followed in the preparation of drug substances or in the carrying out of a clinical trial. This system is intended to ensure consistency and quality
<b>Quality Control (QC)</b>	The examination and certification of a substance to establish that it conforms to the previously defined specification
<b>Radiolabelling</b>	The process by which a molecule is enriched in an unstable isotope to enable its easy detection at extremely low levels in biological samples
<b>Radioligand</b>	A ligand which contains a radioactive atom to enable its binding to a receptor to be readily monitored on a small scale, for example, using a scintillation counter.
<b>Randomisation</b>	An unbiased procedure by which subjects are assigned to either drug or placebo arms of a clinical trial
<b>Rat sarcoma protein (ras)</b>	A family of proteins is found in all cell lineages and are involved in cell signalling. They belong to the small GTPase class of proteins; overactive Ras signalling can lead to cancer.
<b>Reactive metabolites</b>	Possibly damaging molecules arising from the metabolism of a drug
<b>Receptor</b>	A naturally occurring protein with which a ligand interacts to cause an effect in a biological system

Term	Description
<b>Receptor domains</b>	Different and distinct regions of a receptor which have different characteristics
<b>Receptor tone</b>	That amount of signal transmitted by a receptor in the absence of natural ligand or agonist (see Constitutive Activity)
<b>Reductases</b>	A class of enzymes which catalyse the reduction of biomolecules or functional motifs such as carbonyls, double bonds and nitro groups.
<b>Registration</b>	The process whereby a regulatory authority, eg the FDA assesses the pharmacological and clinical data on a new medicine and grants the developer a licence to market it.
<b>Regulatory authorities</b>	Government departments charged with ensuring that new drugs have been fully investigated to show that they do possess the claimed activity without damaging side effects. In addition they are charged with ensuring that unwanted effects appearing in marketed drugs are fully investigated and ordering the withdrawing of drugs for which the long term safety profile or cost-benefit analysis are not acceptable.
<b>Relative bioavailability</b>	The bioavailability of one formulation of a drug compared to that of another
<b>Renal tubule</b>	A portion of the nephron, the basic structural and functional unit of the kidney, which contains the tubular fluid filtered by the glomerulus.
<b>Reporter assay</b>	An assay in which a reporter gene, for, for example, green phosphorescent protein or luciferase, is attached to a gene of interest so that compounds affecting these genes can be readily detected

Term	Description
<b>Reproductive Toxicology</b>	Studies undertaken in non-human mammals to establish the likelihood of an administered substance adversely affecting the reproductive process in the human
<b>Retinoid receptors (RXR)</b>	A class of nuclear receptors which bind retinoids
<b>Retinoids</b>	A class of compounds, including retinoic acid, related to vitamin A which regulate epithelial cell growth and act as transcription factors
<b>Retroviruses</b>	A class of viruses which use RNA as their genetic material. They use an enzyme, reverse transcriptase, to generate DNA which is then inserted into the genome of an infected cell.
<b>Reverse transcriptase</b>	An enzyme used to generate complementary DNA from viral RNA. Inhibitors of this enzyme are widely used as anti-retroviral drugs.
<b>Reverse transcription polymerase chain reaction (RT-PCR)</b>	An amplification technique used in molecular biology to detect RNA expression levels by creation of cDNA from RNA by the polymerase chain reaction.
<b>Reversible</b>	In the context of medicinal chemistry, a process such as receptor interaction or enzyme inhibition which returns to the previous condition on the removal of the ligand
<b>Rhodopsin family</b>	A family of transmembrane globular proteins that comprise the largest group of G-protein coupled receptors. They have been subdivided into at least 19 groups, for ligands including proteins, neurotransmitters, fatty acids, phospholipids, cannabinoids and prostaglandins

Term	Description
<b>Ribosome</b>	A complex structure found in all cells on which proteins are synthesised from their constituent amino acids. It consists of two parts, one of which recognises the transfer RNA molecules linked to the amino acids and another on which coupling of the amino acids takes place thus giving peptides and proteins.
<b>RNA Interference (RNAi)</b>	The use of natural or synthetic low molecular weight RNAs, microRNA and small interference RNA, to bind to messenger RNA and thus block expression of specific genes and protein synthesis
<b>Sarcoma</b>	A cancer which arises in transformed cells of bone, cartilage, fat, muscle and vascular and hematopoietic tissues.
<b>Scatchard plot</b>	This is a method of analysing the data for freely reversible ligand / receptor binding interactions. It graphically represents the ratio of concentrations of bound ligand to unbound ligand against the bound ligand concentration.
<b>Schild equation</b>	A mathematical analysis of drug-receptor binding of agonists and antagonists from which it is possible to determine the nature of the binding and the presence of more than one type of receptor $r = 1 + x/K_B$
<b>Scintillation proximity assay (SPA)</b>	An assay in which microscopic beads containing a scintillant are coated with a preparation of the biological target, eg enzyme, antibody or receptor, of interest. Binding of a radiolabelled potential ligand to the target so that it is in close proximity to the scintillant causes the release of light which can be readily detected and measured.
<b>Screening</b>	The evaluation of a series of compounds to establish their activity in a designated assay.
<b>Screening cascade</b>	The progressive series of tests used to select a compound for further study as a drug candidate

Term	Description
<b>Screening library</b>	A collection of compounds to be tested for their activity in designated assays
<b>Second messenger</b>	Molecules, usually proteins, which, following the initial binding of agonists to surface receptors, are released into the intracellular compartment, to elicit the biological response
<b>Secretin</b>	A family of evolutionary related membrane proteins all of which have seven transmembrane sections and act as receptors for a wide range of hormones including glucagon
<b>Secretory mechanism</b>	The process whereby biologically active compounds, especially hormones, are released from cells and glands
<b>Selectivity</b>	A measure of the ability of a molecule to preferentially interact with a specific biological system.
<b>Sensory nervous system</b>	One arm of the peripheral nervous system that detects sensory information from touch, sound, taste, smell, vision and balance.
<b>Serious Adverse Event (SAE)</b>	The observation in a volunteer or a patient of an unexpected effect of dosing a drug, which may or not be drug related and which could have serious consequences unless dosing is stopped immediately
<b>Serum albumin</b>	A globular protein produced in the liver which is present as the most abundant protein in blood plasma. It carries hydrophobic steroids and other drugs around the blood circulation.

<b>Term</b>	<b>Description</b>
<b>Side effects</b>	Biological effects of drugs other than those for which the drug was designed. These can be both harmful or beneficial.
<b>Silent Agonist</b>	A molecule which binds into a receptor and puts it in a desensitised state with little or no apparent efficacy. Subsequent allosteric binding by another modulator then gives activation.
<b>Silent Antagonist</b>	A competitive receptor antagonist with zero intrinsic activity. The terminology was introduced to distinguish this class of molecule from those which are partial or inverse agonists
<b>Single compartment model</b>	A mathematical model of drug pharmacokinetics in which it is assumed that the drug is distributed instantaneously into a single compartment
<b>Site of action</b>	The part of the body at which a particular drug exerts its effects.
<b>Small Molecules</b>	Molecules constructed by chemical synthesis, as opposed to biological processes, which typically have molecular weights of 250 - 750 Da
<b>Specific binding</b>	In a radiolabelled ligand binding assay, specific binding involves interaction with the target receptor. In contrast, non-specific binding involves interaction with everything else, for example other proteins in the tissue, the assay vessel etc.
<b>Spinal cord</b>	A long thin bundle of nerves contained within the spine which is responsible for carrying electrical impulses to and from the brain to other parts of the body.

Term	Description
<b>Spray-dry</b>	A technique used in pharmaceutical development for the drying of fine powders prior to formulation. This can result in a smaller particle size and therefore enhanced solubility
<b>Src</b>	A proto-oncogene encoding a non-receptor tyrosine kinase which is an important signalling protein
<b>Src homology (domain) (SH2)</b>	A protein domain initially identified in the Src oncoprotein but now found in many other intracellular signal-transducing proteins, which allows them to dock with phosphorylated tyrosine residues on other proteins.
<b>Standard Operating Procedure (SOP)</b>	A formally approved written procedure for carrying out repeat processes safely and reliably
<b>Stem cell (sc)</b>	Progenitor cells which which have the potential to proliferate and differentiate into other cell types in order to replenish or repair damage to the parent tissue.
<b>Structure Based Drug Design (SBDD)</b>	Drug design based on a knowledge of the structure of the target and/or the target-ligand complex.
<b>Structure-Activity Relationships</b>	The relationship between changes in the chemical structure of a group of molecules and their biological properties
<b>Subcutaneous dosing</b>	An injection of a drug into the fat layer between the skin and the muscle.

Term	Description
<b>Super Agonist</b>	An agonist molecule which is capable of producing a maximal response which is greater than that of the natural ligand for that receptor.
<b>Sustained release</b>	A particular formulation of a drug in which the active agent is released gradually over an extended period of time, thus giving sustained biological activity.
<b>Sympathetic nervous system</b>	A subdivision of the autonomic nervous system which maintains homeostasis, and is also responsible for initiating the 'flight or fight' response
<b>Synaptic cleft</b>	The gap between the part of the neurone that releases its neurotransmitter and the part of the neurone that carries the receptor. The neurotransmitter passes across the synaptic cleft thus maintaining the nerve impulse.
<b>T wave</b>	A deflection in the electrocardiogram which represents ventricular repolarisation of the heart.
<b>Tanimoto similarity</b>	A mathematical method used to compare one set of compounds to another by analysis of fingerprints, which comprise constituent atoms, connectivity and functional groups. It is used to evaluate libraries, both real and virtual, to find new lead compounds.
<b>Target</b>	The particular part of the body against which a drug is designed to act. This can be either a discrete biomolecule, a biochemical pathway, or a specific organ within the body.
<b>Target Selection</b>	The establishment of a correlation of a disease with a specific biological target and its use to discover new treatments

Term	Description
<b>Target Validation</b>	Confirmation, as far as is possible, of the relationship between a specific molecular target (or pathway) and a disease state or symptom such that molecules interacting appropriately with the target can be expected to modify the disease.
<b>Teratogen</b>	A chemical which is capable of causing damage to the developing foetus.
<b>Terminal half-life</b>	The time taken for the plasma concentration of a drug to fall by 50%, and ideally assessed following intravenous administration. The fall in concentration is due to metabolism and clearance / excretion processes.
<b>Therapeutic area</b>	A group of diseases categorised by the observed symptoms, for example metabolic disease, heart disease etc.
<b>Therapeutic class</b>	A group of molecules / drugs which are used to treat the same diseases.
<b>Therapeutic effect</b>	The intended, and beneficial result of the action of a drug on a patient.
<b>Therapeutic index</b>	The ratio of the dose of a drug that causes its therapeutic effect relative to the amount that causes an adverse event, such as toxicity in animals or serious adverse effects in humans
<b>Therapeutic window</b>	The range of doses, and consequently of plasma levels, between which an administered drug exerts its required effects without inducing unwanted side effects.

<b>Term</b>	<b>Description</b>
<b>Thermodynamic solubility</b>	An expression of the concentration of a substance in a solvent under equilibrium conditions
<b>Tissue</b>	A cellular complex intermediate in organisation between a cell and a complete organ.
<b>t<sub>max</sub></b>	The time at which the plasma concentration of drug reaches its maximum level after administration
<b>Tool Compound</b>	A compound whose properties have not been optimised, but which nonetheless exerts a pharmacological effect that can be studied.
<b>Toxicity</b>	Harmful effects of exogenous materials including drugs and their metabolites.
<b>Toxicokinetics</b>	The study of the variation with time of the concentration of the administered substance in the blood stream following the administration of a substance, at doses used in toxicology studies
<b>Toxin</b>	A poisonous substance produced within living cells or organisms
<b>Transcellular absorption</b>	The passive absorption of a drug molecule across a biological membrane through the cells by diffusion, by use of an active carrier and transcytosis.

Term	Description
<b>Transcellular fluid</b>	Body fluids such as cerebrospinal, ocular and joint fluids which are found in epithelial lined spaces. These comprise approximately 2.5% of the total body water
<b>Transcription</b>	The first stage of the process whereby the cell's genetic information is converted to a protein structure, and which takes place in the nucleus. A complementary RNA strand is constructed by the action of RNA polymerases on one chain of the DNA and this is used in the next stage of protein synthesis, namely translation.
<b>Transcription factors</b>	Biomolecules (usually proteins) which bind to specific regions of DNA and initiate gene expression
<b>Transcytosis</b>	The transport process whereby macromolecules are captured into vesicles on one side of the cell. This moves through the cell and is expelled along with the macromolecule on the other side.
<b>Transduction mechanism</b>	The intracellular signalling process which takes place after an extracellular molecule binds to a cell surface receptor
<b>Transformation</b>	In molecular biology, the process of genetically altering a cell by the incorporation of extracellular DNA.
<b>Translation</b>	The second stage of the process of conversion of genetic information in the gene to specific proteins. Single-stranded messenger RNA molecules generated in the transcription stage bind to the ribosome and are then targetted by transfer RNA molecules carrying particular amino acids, coupling of which gradually builds up the new protein.
<b>Transmembrane domain</b>	The region of a transmembrane protein lying within the membrane.

Term	Description
<b>Transmembrane helices</b>	In a transmembrane protein the helical structures lying within the membrane
<b>Transmembrane protein</b>	A protein which is located in the cell membrane such that one end of the protein chain lies inside the cell and the other outside it.
<b>Transpeptidases</b>	An enzyme that catalyses the transfer of an amino acid or peptide group from one protein to another
<b>Transport (of drug)</b>	Passive transport of drugs involves diffusion down a concentration gradient; active transport (eg involving drug transporters) requires energy (e.g. ATP)
<b>Transporters</b>	Drug transporters are multiprotein complexes in the cell membrane which facilitate influx and efflux of molecules, including drug molecules to and from the cell
<b>Turnover</b>	In drug metabolism the extent to which parent compound is lost as a function of time
<b>Two compartment model</b>	A modelling approach to the pharmacokinetics of a drug which assumes that the body can be regarded as being comprised of two compartments, one known as the central compartment with good blood supply and the other, the peripheral compartment with lower blood flow. Equations to predict the pharmacokinetics of a drug can be derived from combinations of the pharmacokinetics in each of the two compartments.
<b>Two state model</b>	A model of receptor action in which it is hypothesised that the receptor can exist in two conformations, one active and the other inactive. An agonist will then bind to the active conformation resulting in the initiation of the biological response and a shift in the equilibrium between the conformers in favour of the active form

Term	Description
<b>Type 1 human adverse drug reactions</b>	Side effects of the use of drugs which might be anticipated based on the mode of action of the drugs
<b>Type 2 human adverse drug reactions</b>	Idiosyncratic, or unexpected side effects resulting from the clinical use of drugs
<b>Tyrosine kinase domain</b>	The conserved protein sequence containing the catalytically active site of the tyrosine kinases
<b>Ubiquitin</b>	A small (8.5kDa) regulatory cellular protein which is added to larger proteins for a number of purposes. These include signalling for degradation, alteration in cellular location / activity and protein-protein interactions.
<b>Uncompetitive Inhibitor</b>	A compound which inhibits an enzyme by binding to the enzyme/substrate complex
<b>Veber's Rules</b>	A categorisation of the molecular properties (related to Lipinski's) that influence the oral bioavailability of a drug molecule
<b>Vesicle</b>	A membrane bound structure within a cell in which materials such as enzymes are transported or stored.
<b>Virus</b>	A small infectious entity that can only replicate inside a target cell.

Term	Description
<b>Volume of distribution</b>	A concept which can be used to quantify the distribution of a drug in the body after extravascular dosing. It is the theoretical volume in which the drug would need to be uniformly distributed to produce the observed blood concentration
<b>Voluntary nervous system</b>	The part of the peripheral nervous system that is under the conscious control of the individual.
<b>Western blot</b>	A technique used in molecular biology for the detection, analysis and quantification of specific proteins in tissue extracts or homogenates. Proteins from the homogenate are first separated by gel electrophoresis and identified by binding to specific radiolabelled antibodies.
<b>Wild-type (gene)</b>	The most common non-mutated form of a gene. It is the form that leads to the most often observed phenotype of the organism.
<b>Xenobiotic</b>	Any chemical in the body which has not been made by that organism and is therefore foreign to it. It includes food, drugs and toxins.
<b>Z' Factor</b>	The Z' factor quantifies the robustness of results from a high throughput screen based on the statistical spread of activity of the positive and negative controls (pc and nc respectively). The closer Z' is to unity, the more robust the assay. $Z' = 1 - [3 (\Delta SD_{pc-nc}) / \Delta mean_{pc-nc}]$
<b>Zn peptidases</b>	A peptidase enzyme which cleaves the terminal amide bond of a protein or a peptide and which has a zinc atom complexed in the active site. It functions at neutral pH.
<b>Zwitterion</b>	A molecule which has both a negatively and a positively charged group and thus has overall a formally neutral structure.