Short Glossary of Terms (Version 1.3 of the MeduMaZe Drug Development & Approval Game; the most important ones are shown in BOLD type)

Acronym or Descriptive Term	Definition and Description
Early Discovery & Development	Research chemists and biologists search for new disease area targets for synthesized compounds based on developing knowledge about biochemical pathways. Experiments in vitro and in laboratory animals look for primary (desirable effects, or efficacy) and secondary (undesirable 'side' effects) pharmacological properties as well as studying the basic toxicology of the compound. Pharmaceutical scientists determine whether the chemical and physical properties of the compound are favorable to manufacture of drug substance and a finished formulation. Clinical research scientists start to plan for Phase 1 – First-in-Human studies. Regulatory specialists help the team develop a plan to bring the product to market; marketing evaluate the characteristics of a product that would meet the needs of patients and healthcare professionals, and would recoup the R&D investment.
Development & Clinical Studies	Government agency and independent ethics committee review of the data generated so far and the proposed clinical study(ies) are required before the compound is tested in humans. Initial studies are short and may only involve a single dose to human volunteers or patients, later studies in patients may span months or years, depending on whether the drug will be used for a short time (e.g. antibiotic) or be taken chronically (e.g. Alzheimer's). As appropriate to the type of product, indication, duration of use and route of administration, toxicology studies confirm that there is no hidden risk of birth or growth defects or cancer associated with taking the drug. Pharmaceutical scientists ensure that the product can be manufactured efficiently and economically and that it may be stored safely by pharmacies and patients.
Regulatory Review & Approval	When the sponsor of the drug is sure that they have proof of Quality, Safety and Efficacy for at least one formulation and indication, they will submit a 'Marketing application' to the government agencies in each country for an independent assessment of the data. Once reviewed and approved, the drug may be marketed as soon as a price has been agreed.
Accelerated Approval Pathways	These are programmes administered by regulatory agencies to expediate the availability of important new medicines to patients. They are tailored to the stage of development and some offer incentives in terms to speed of approval or intellectual property. Examples include: UK: Innovative Licensing and Access Pathway (ILAP), Innovation Passport, Project Orbis, Conditional Marketing Approval US: Orphan Drug Designation, Accelerated Approval, Breakthrough Therapy, Fast Track, Priority Review EU: accelerated assessment, Conditional Marketing Approval, Orphan Drug, Paediatric Use Marketing Authorisation, PRIME
Adaptive Designs	A clinical trial design that allows for prospectively planned modifications to the study based on an interim analysis of accumulating data. These designs can be useful for various types of trials, including early-phase exploratory trials and dose-ranging studies in humans.
ADME	Absorption, Distribution, Metabolism and Excretion. How the body takes up the drug, where it goes in the body, and how it is eliminated, ADME studies describe the pharmacokinetics (PK) and bioavailability of a compound. For example, following administration of a radiolabeled version of the drug to human volunteer(s) in a mass balance study, excreta (urine, faeces) is collected over a defined period of time and the content of radiolabel in the excreta over time is used to confirm the rate and extent of absorption, distribution/disposition, metabolism and excretion.
Ames Test	An *in vitro* test for gene mutation in bacteria, one of a standard battery of tests for mutagenicity.

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Amorphous	Lacking a distinct crystalline structure.
AMS	Accelerated mass spectrometry (AMS) is an analytical tool with high selectivity, sensitivity and precision. It has a variety of applications including radiocarbon dating, forensics and biomedical, especially for Mass Balance (ADME) and Microdosing (Phase 0) clinical trials in human subjects. Following separation of the rare ^{14}C isotope from the stable ^{12}C isotope, the measured ratios of the two isotopes (abundance sensitivity) are used to quantify radioactive (drug-related) material. Around 10% of the ^{14}C in a sample is counted; this is 1000-times more efficient than decay counting.
Basket Trials	A basket (or bucket) clinical trial tests the efficacy and safety of a new drug or biologic in patients who have different types of cancer but share the same mutation or biomarker. It is a development acceleration strategy that has been widely adopted in Oncology since a seminal Phase I clinical trial in patients with advanced solid tumours in 2010 - the KEYNOTE-001 Study of Pembrolizumab.
Biological	A biological product is any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of humans. Examples include monoclonal antibodies, vaccines and gene therapies.
BLA	A Biologics License Application is submitted to the US FDA to obtain approval for manufacture and marketing of a biologic product intended for use in humans. See also NDA, MAA.
Biomarker	An objectively measureable indicator used to determine how well the body responds to a treatment for a disease or condition, or how a disease has progressed. Examples include receptor proteins, clinical biochemistry analytes or genes.
Blood Dyscrasias	A general term used to describe an abnormality in the blood or bone marrow's cellular components, e.g., low white blood cell count, low red blood cell count or low platelet count.
Carcinogenicity	The type of toxicology study intended to detect the potential of a drug to cause cancer in humans. These studies involve chronic dosing of the drug to mice and/or rats for 18 to 24 months. They are also referred to as “oncogenicity studies”. Historically required for all small molecule drugs intended for chronic administration to patients for more than 6 months or intermittently for recurrent conditions but not usually required for Oncology drugs or for Biological products.
Centralised Procedure	A European Union registration procedure created by Council Regulation (EEC) No. 726/2004 for the authorization of medicinal products, for which there is a single application, a single evaluation and a single authorisation allowing direct access to all European Union Member States. Applications are submitted directly to the European Medicines Agency (EMA). The single scientific evaluation is made by a review team lead by a Rapporteur and Co-rapporteur on behalf of all EU Member States. The opinion of the CHMP is transmitted to the European Commission and transformed into a single Marketing Authorisation applicable to the whole European Union. his procedure is compulsory for medicinal

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Acronym or Descriptive Term	Definition and Description
	products derived from biotechnology, new active substances for treatment of HIV, cancer, neurodegenerative disorders, diabetes, viral diseases, auto-immune diseases and other immune dysfunctions, advanced therapy medicines such as tissue-engineered or gene therapy, orphan medicines, and is optional for other new medicinal products.
CFR	The Code of Federal Regulations is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the US Federal Government, such as FDA.
CHMP	The Committee for Human Medicinal Products is the senior scientific committee charged with review and evaluation of new medicines in Europe and with formulating the opinion of the European Medicines Agency (EMA). Each member of the CHMP is drawn from a European Union Member State medicines regulatory agency.
Clinical Hold	A clinical hold is an order issued by the US FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation, usually on safety grounds. In the EU, a Member State may also suspend or prohibit a clinical trial.
Common Technical Document	The Common Technical Document or CTD is an agreed format and organizational structure for the Chemistry Manufacturing and Controls data, Nonclinical and Clinical study reports, and summaries, that constitute a national or regional marketing application (e.g., MAA, BLA, NDA). In most countries, CTDs are submitted in electronic format (eCTD)
Co-rapporteur	In the European Union Centralised procedure for review of a new drug or biological, a Rapporteur and Co-rapporteur are assigned to coordinate the scientific review of the marketing application. Both the Rapporteur (lead) and Co-rapporteur are members of the Committee for Human Medicinal Products (CHMP). See also Centralised Procedure, EMA.
Cost of Goods	The cost of manufacture of a finished drug product, including the active ingredient, any excipients, and both the primary and secondary packaging materials.
Crossover Study	A clinical trial design in which each subject receives each treatment e.g., half the group receives active drug and half the group receives placebo; then after a washout period the subjects who received active receive placebo and those that received placebo receive active. Thus each subject serves as his or her own control.
CTA	A Clinical Trial Application is the regulatory submission, based on summary data, made to European Union, UK, and Canadian regulatory agencies to obtain approval to initiate a new clinical trial.
Cytochrome P450 (CYP) Enzymes	A group of mixed function mono-oxidase enzymes that metabolise many drugs – their activity may influence the plasma level, efficacy and side effects in different individuals. Understanding which enzymes are involved in the metabolism of a compound in development is very

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	helpful when assessing its potential for Drug Interactions.
Decentralized	Introduced in 2006, this process supersedes the Mutual Recognition process for marketing approval in the EU. An MAA is submitted to a Reference Member State for review, with copies provided to all Concerned Member States.
Decision	In the context of the European Centralised Procedure, the final Decision on whether a product is granted a marketing authorization is made by the European Commission, and that Decision is binding on all Member States.
Double-blind	A clinical trial design in which neither the patient, nor the investigators, or sponsor staff involved in the treatment or clinical evaluation of the subjects, are aware of which treatment individual patients have received (e.g., who received active drug and who received placebo). This includes anyone determining subject eligibility, evaluating endpoints, or assessing compliance with the protocol, throughout the conduct of the trial. Only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded to treatment assignments.
Double-dummy	A clinical trial design which is useful when the test drug (or its comparator) is presented in a distinctive container or delivery system or has a physical characteristic (e.g., colour) which cannot be presented to the patient in a blinded manner, such that a 'dummy' of each treatment is needed to maintain the blind.
Drug Interactions	Drugs are broken down (metabolized) via a variety of biochemical routes so that they can be eliminated from the body in the urine or faeces. These biochemical routes, especially those catalyzed by enzymes (see Cytochrome P450), can be inhibited, activated, or induced by concomitant treatment with another drug. This can alter the blood or tissue levels of both drugs – sometimes increasing exposure of the drugs or their metabolites to toxic levels, and sometimes decreasing exposure to less than efficacious levels. Understanding the potential of the drug to interact with other common medicines or those that are known to use the same biochemical routes of elimination is an important objective of Drug Interaction studies, usually conducted in human volunteers following preliminary studies *in vitro* or in animals.
DSUR	Development Safety Update Report. A periodic analysis of new nonclinical and clinical safety information gathered during a clinical trial programme to support an ongoing assessment of the risk to trial subjects.
Efficacy/ Effectiveness	The measurement of a drug's desired influence on a specific disease state and its power to produce a result. Efficacy is what occurs during ideal or experimental conditions; effectiveness is what occurs under conditions of real use.
Efficacy Pharmacology	Animal pharmacology studies intended to assess the potential of a drug to have its desired pharmacological effect on a biological system or disease. These do not have to be conducted to GLP.
EMA	European Medicines Agency – responsible for coordinating the scientific evaluation and supervision of medicinal products under the

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	Centralised Procedure in the EU.
End of Phase 2 Meeting	In the US, a sponsor is entitled to meet with the FDA Review Division at the end of Phase 2 to obtain scientific input before the progression to Phase 3.
EPAR	European Public Assessment Reports are publicly available summaries of CHMP's review and opinion regarding any product submitted to EMA for review under the Centralised Procedure that is approved for marketing by the European Commission. Somewhat analogous to the US Summary Basis of Approval.
Estimand	Statistical terminology for the treatment effect that a clinical trial is designed to measure, taking into account the research question/study objectives, the desired clinical endpoints, their relevance, variability and measurability, the statistical power and design of the study, the overall analysis plan and any sensitivity analyses.
Ethics Committee	An independent review body for clinical study protocols which considers and approves or declines to approve biomedical research involving human subjects. The Committee will review, approve the initiation of, and conduct a periodic review of the clinical research conducted at that institution. The primary purpose of the review is to assure the protection of the rights and welfare of the human subjects. In the US the analogous term is Institutional Review Board (IRB).
EU Filing Route	A strategic decision about whether a product should be submitted and reviewed under the Centralised Procedure or the Decentralized Procedure in the EU. For some products, the Centralised Procedure is mandatory; for others many factors need to be taken into consideration.
European Commission	The executive organ of the European Community which proposes policy and legislation and conducts bureaucratic and administrative activities which have pan-European impacts, e.g., the final approval of a MAA for a new product to be approved in all EU Member States via the Centralised Procedure.
Fast Track	A US program where the applicant proposes to FDA, during the IND phase, that the product appears to address an unmet medical need with respect to a serious or life-threatening disease. FDA has defined an unmet medical need as a "medical need that is not addressed adequately by an existing therapy". Fast Track status allows the applicant more opportunities for dialogue with FDA during development and the potential to submit portions of the NDA in advance but does not guarantee an Accelerated Review for the NDA.
FDA	Food and Drug Administration, the US medicines regulatory agency.
FDA Inspection	The US FDA (like most other regulatory agencies) has the right to inspect sponsor and investigational facilities to confirm that data presented

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	in support of a marketing application has been generated according to the relevant GXPs.
GCP	Good Clinical Practice. This is a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials to provide assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. The ICH GCP guidance provides a unified, global standard to facilitate mutual acceptance of clinical data by the regulatory authorities in different countries.
GLP	Good Laboratory Practice. These are standards for conducting nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for food and color additives, animal food additives, human and animal drugs, medical devices for human use, biological products, and electronic products. Compliance is intended to assure the quality and integrity of these data. GLPs cover topics such as animal care and documentation, lab methods, procedures, archiving of information and independent review by a quality assurance unit. Animal toxicology studies are conducted according to GLP.
GMP	Good Manufacturing Practice. These standards concern the design and construction of pharmaceutical plants and their operation and address the manufacture, processing, packing, release and holding of a drug, including packaging and labeling, operations, testing and quality control of a drug product or biological.
Guidelines	These documents are issued by the regulatory agencies of each country or region, or by the ICH, to provide guidance on practical aspects of testing, preparation of regulatory submissions and current scientific thinking on emerging topics. They are not legally binding but sponsors are expected to consult guidances and follow them wherever scientifically feasible.
Health Technology Assessment	The assessment of whether a new medicine, diagnostic or device represents an advance over existing alternatives to the extent that it should be made available through national health services (e.g., NICE in UK). This so-called 'fourth hurdle' is separate to the evaluation of safety, quality and efficacy conducted by the medicines regulatory agency (e.g., MHRA in UK).
hERG Testing	Compounds associated with adverse drug reactions of QT prolongation in humans, arrhythmias such as torsades de pointes (TdP) and sudden death often have a secondary pharmacological interaction with the potassium channel K_r . The gene encoding this channel has been identified as hERG (human *ether-a-go-go* related gene). Testing compounds for interactions with the hERG channel can be used as an *in vitro* screen to identify the potential risk of QT prolongation.

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ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – its global mission is to ensure that safe, effective and high quality medicines are developed, registered and maintained in the most resource efficient manner whilst meeting high standards
Inclusion/ Exclusion Criteria	The protocol for a clinical study will include 'rules' or criteria that help to define the patient population under study and thus minimize variability in results due to factors other than the effects of the drug. For example, inclusion criteria might confirm that all patients have the same disease at the same severity, and exclusion criteria might prevent patients who are taking certain other medications or who have other diseases, women who might become pregnant, or patients under/over a certain age group from participating until safety data is available to support their inclusion. The further along in clinical development and the larger the studies, the less restrictive these criteria should be, to ensure that the patients recruited to trials are representative of the real-world.
IND	In the US, an Investigational New Drug Application is required to permit the sponsor to conduct clinical trials that may be used to support a future NDA and to ship investigational drug across state or national borders. Over time, a sponsor will submit many reports and clinical trial protocols to a single IND.
International Non-Proprietary Name	The International Non-Proprietary Name, or INN, is proposed by the sponsor and approved by the World Health Organization. It is the generic name used to describe the product in product labeling and publications. It cannot be trademarked and it must include a stem that denotes its chemical class.
Investigator's Brochure	This compilation of all currently available nonclinical and clinical information about a product under investigation in humans is intended to inform Clinical Investigators who are conducting trials about the likely risks and benefits of the product they are using. It should be regularly reviewed and updated as new data are generated.
Liver Enzymes	Alanine aminotransferases (ALT, also known as SGPT), aspartate aminotransferases (AST, also known as SGOT) and alkaline phosphatase (ALP). These are usually monitored throughout clinical trials as a biomarker for potential liver damage.
MAA	Marketing Authorization Application (UK, Europe, Australia, New Zealand and South Africa). Analogous to a US NDA or BLA.
Marketing Application	The submission of detailed quality (Chemistry, Manufacturing and Controls), safety (nonclinical and clinical) and efficacy (clinical) data to an independent Regulatory Agency in order for them to conduct a review of the suitability of the product for marketing. See also MAA, BLA, NDA, and CTD.
MedDRA	The Medical Dictionary for Regulatory Activities is a rich and highly specific standardised medical terminology developed by ICH to facilitate sharing of regulatory information internationally for medical products used by humans. For example, it is used to code adverse events and

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Acronym or Descriptive Term	Definition and Description
	look for safety signals.
MHRA	Medicines and Healthcare Products Regulatory Agency, the UK medicines regulatory agency.
Microdosing trials	This is an approach to conduct of exploratory clinical trials in humans which involve very limited human exposure, have no therapeutic intent, and are not intended to examine clinical tolerability and safety, but which may provide data on pharmacokinetics, pharmacology and biomarkers.
Mouse Micronucleus Test	An *in vivo* test for chromosomal damage using mouse hematopoietic cells, one of a standard battery of tests for mutagenicity
Mutagenicity	Mutagenicity or Genotoxicity tests are *in vitro* and *in vivo* tests designed to detect compounds that induce genetic damage directly or indirectly by various mechanisms. These tests help sponsors and regulatory agencies identify the potential for a drug to damage DNA and its fixation, and induce cancer and/or heritable defects. Testing usually includes (i) A test for gene mutation in bacteria, (ii) An *in vitro* test with cytogenetic evaluation of chromosomal damage with mammalian cells or an *in vitro* mouse lymphoma tk assay and (iii) An in *vivo* test for chromosomal damage using rodent hematopoietic cells. If tests show a positive result, additional assessment will be needed to establish a 'weight of evidence' determination regarding the risk of mutagenesis. In some cases a positive result effectively ends development of the compound.
NDA	In the US, a New Drug Application is submitted to the FDA to obtain approval to market a new chemical entity or drug (see BLA for biological products). Analogous to a UK or European MAA.
Nitrosamines	Chemical compounds classified as probable human carcinogens and sometimes encountered as impurities in drug substances or excipients, or as extractables from packaging or manufacturing equipment.
OJ	The Official Journal of the European Communities, in which new European Legislation is published.
-omics	High throughput methods and technologies for supporting drug discovery, including genomics (study of the genome), proteomics (study of proteins), transcriptomics (study of RNA transcripts) and metabolomics (study of metabolites).
Orphan Drug	Orphan drugs are products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. According to the World Health Organization's estimates, around 5,000 rare diseases affect human beings on a worldwide scale. In the US, rare is defined as a disease or condition that affects fewer than 200,000 people in the United States. In the European Union the prevalence is defined as a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. A variety of incentives to encourage the study of medicines to treat these diseases are available to sponsors, including the opportunity to discuss and agree abbreviated or

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	unconventional development programs.
Package Insert	The Package Insert (or PI) is the FDA-approved text that contains the most important information needed by a prescribing physician in order to make a decision on the suitability of a particular drug for a particular patient. The PI summarizes key efficacy, safety and risk:benefit information about the product. It is somewhat analogous to the SmPC in the EU.
Parallel Group Design	A common approach to Phase 2 and 3 clinical studies where two (or more) groups of patients receive treatment at the same time so that treatments can be directly compared. Thus patients are randomised to one of two (or more) arms, and each arm is allocated a different treatment. Treatments will include the investigational product at one or more doses, and one (or more) controls, such as placebo and/or an active comparator.
Patient Instruction Leaflet	Information written in patient-friendly language to help patients use their medicines correctly. It is approved along with the EU SmPC as part of the MAA.
Patient Registry	An organized system that collects clinical and other data in a standardized format for a population defined by a particular disease (e.g. to understand the Natural History of the disease in a particular region) or condition (e.g. Rare or Orphan indication) or drug exposure (e.g. a pregnancy registry as part of a Risk Management Plan). These can be important sources of Real-World Data.
Paediatric	Drugs may be metabolized and eliminated differently by children. Clinical studies should include a representative sample of all age groups that suffer the disease of interest, including paediatric patients (there are regional differences in definitions but paediatrics are generally considered to be less than 16 years of age).
PBPK	Physiologically-Based Pharmacokinetic (PBPK) modeling; used to model the likely rate and extent of exposure to an administered dose at different timepoints.
PGP Inhibitor or Substrate	PGP or p-glycoproteins are part of a larger family of efflux transporters found in the gut, gonads, kidneys, biliary system, brain and other organs. They transport certain hydrophobic substance into the gut, out of the brain, into urine or into bile. PGPs play a large role in the distribution and elimination of many clinically important therapeutic substances. It is helpful to determine whether a drug may act as a PGP inhibitor or substrate.
Pharmacokinetics	The study (rate and extent) of what the body does to a drug.
Pharmacodynamics	The study of what a drug does to the body.
Pharmacogenetics	The study of how your genes affect the way your body responds to a medicine. Pharmacogenetics information may predict a patient's

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	suitability for a particular medicine, or the most appropriate dose.
Pharmacovigilance	The ongoing monitoring and review of clinical safety information arising during clinical trials and post-marketing surveillance.
Phase 0	See Microdosing trials, sometimes these are the First-in-Human studies.
Phase 1	Phase 1 clinical studies typically include the first administration of a new drug or biologic into humans. They are closely monitored and may be conducted in patients or volunteers. Early studies are designed to determine the pharmacologic effects and pharmacokinetics of the drug in humans, the side effects associated with increasing or repeated doses, and, perhaps, to gain early evidence on efficacy. They may include elements of adaptive design and should have clear stopping rules. During Phase 1, sufficient information about the pharmacokinetics and pharmacological effects of the drug should be obtained to permit the design of well-controlled, scientifically valid Phase 2 studies. Phase 1 studies also include studies of drug metabolism, pharmacokinetics in normal, renally or hepatically-impaired subjects, the potential for Drug Interactions, food effects, and studies where drugs are used as research tools to explore the value of Biomarkers, biological phenomena or disease processes. The total number of subjects included in Phase 1 studies varies with the drug, but is generally in the range of 50 to 100.
Phase 2	Phase 2 includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for an indication in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are usually conducted in 200-400 subjects; typically, these are randomized, controlled, parallel group, double-blind studies and may include elements of adaptive design. Typically, the most detailed examinations of dose-response are conducted during Phase 2.
Phase 3	Phase 3 studies are usually large, randomized, controlled, double-blind and, sometimes, uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the confirmatory evidence of efficacy and safety needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for prescribing information. Phase 3 studies usually include hundreds or thousands of subjects. They are typically of a longer duration and in a more diverse patient population than Phase 2 to more closely mimic the intended conditions of use. Phase 3B studies are usually intended to explore expanded indications for the drug, including new dosage regimens or patient populations, or to compare its efficacy with other products.
PIL	Patient Information Leaflet. In the UK and EU, the leaflet that accompanies the medicine, designed to be read by the patient.
Plasma Protein Binding	Binding (usually reversible) of the drug to the proteins in blood or plasma, such as albumin. The degree of binding determines the proportion of free drug available to exert its action on the body.

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Polymorphism	Polymorphism occurs when a compound exhibits different crystalline or amorphous forms or has several crystal forms containing variable amounts of a solvent (solvates) or water (hydrates). Polymorphic forms of a drug substance may have different chemical and physical properties, which can have a direct effect on drug product stability, dissolution, and bioavailability.
Pre-IND Meeting	An opportunity to meet with the US FDA to discuss the proposed clinical study and supporting nonclinical data prior to submission of the formal IND application.
Pre-MAA Meeting	It is possible to request a formal meeting with the MHRA or an EU regulatory agency or with EMA. This opportunity is formalised for products reviewed via the Centralized procedure. Such meetings can be very useful for establishing communication lines and operational details associated with review of an MAA.
Pre-NDA/BLA Meeting	Sponsors are encouraged to request a formal meeting with FDA prior to submitting an NDA. This is very useful for clarifying documentation and analysis needs and avoiding any miscommunications about the suitability of the application and data for its intended purpose.
Prescribing Information	The most important information needed by a prescribing physician in order to make a decision on the suitability of a particular drug for a particular patient. It should summarize the key efficacy, safety and risk:benefit information about the product. See also SmPC.
Primary Efficacy Endpoint	An assessment of the effect of the drug on the human subject that is determined to be the most important measure of efficacy in a particular clinical study. It might be an objective measure, such as blood pressure under a controlled set of conditions, or a subjective measure, such as patient-reported symptom severity. This primary variable should provide a valid and reliable measure of some clinically relevant and important treatment benefit in the patient population under study and it should generally be used when estimating the sample size.
Primary Packaging	The immediate container in which a drug substance or drug product is contained, e.g., the bottle or vial.
Priority Review	On receipt of a marketing application, the US FDA makes a determination about whether the application warrants a Priority Review or a Standard Review. The applicant may make a case for a Priority Review (e.g., if they provide a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious or life-threatening disease) but FDA makes the determination.
QT Prolongation	A delay in cardiac repolarization creates an electrophysiological environment that favors the development of cardiac arrhythmias, most clearly torsade de pointes, but possibly other ventricular arrhythmias as well. This can be caused by some drugs. The potential of a drug in development to delay cardiac repolarization is measured *in vitro* (e.g., hERG test) and *in vivo* (e.g., safety pharmacology studies in conscious dogs and/or studies in human volunteers or patients via measurement of prolongation of the QT interval on the surface electrocardiogram (ECG)). The QT interval represents the duration of ventricular depolarization and subsequent repolarization, beginning at the initiation of the QRS complex and ending where the T wave returns to isoelectric baseline.

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Qualified Person	Legally responsible for certifying that each batch of investigational drug meets GMP and standards for release for use in a clinical trial (UK, EU)
Racemate	A racemate is a compound containing a 50:50 mixture of enantiomers (isomers that are mirror images of each other). If a new racemate appears promising, both enantiomers should be studied separately as early as possible to assess the relevance of stereoisomerism on its effects and fate *in vivo*. If the development of a single enantiomer is to be pursued, the nonclinical metabolism and toxicology studies should be conducted with the relevant enantiomer, rather than the racemic mixture.
Rapporteur	In the European Union Centralised procedure for review of a new drug or biological, a Rapporteur (lead) and Co-rapporteur are assigned to coordinate the scientific review of the marketing application.
RCT	A Randomised Controlled Trial is a rigorous clinical trial design used to generate confirmatory data and determine whether a cause-effect relationship exists between treatment and outcome, or for assessing the cost-effectiveness of a treatment. Trial subjects are allocated at random to receive the medicine under test or an appropriate control (e.g. placebo).
Real-World Data	Real-world data relating to patient health status and /or the delivery of health care routinely collected from a variety of sources. Sometimes this is collected through a Patient Registry. Real-world data can be used to derive clinical evidence about the usage and potential benefits or risks of a medical product. Real-world evidence is increasingly used to help support regulatory decision-making, particularly in Oncology and Orphan Diseases.
Registration Samples	Some regulatory agencies require submission of samples of the product proposed for marketing as part of their review process.
Regulation	European Union legislation that is immediately binding on all EU Member States.
Regulatory Authorities/ Agencies	The governmental bodies charged with conducting an independent assessment of the quality, safety and efficacy data associated with a new clinical trial application or a marketing application.
REMS	Risk Evaluation and Mitigation Strategy – required for some products in the US. Somewhat analogous to Risk Management Plan in UK and EU.
Reports	The methods, all results (positive and negative), discussion and conclusions of a scientific study (e.g., stability, toxicology, clinical) should be presented in a formal report suitable for submission and review by a regulatory authority. In some regions, the agency may re-analyse the data, so raw data (e.g., individual human data, individual animal data) should also be made available.
Reprotoxicology	The aim of reproduction toxicity studies is to reveal any effect of one or more active substance(s) on mammalian reproduction through the conduct of studies in rodents, and the extrapolation of those results to humans.

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Rescue Medication	The provision of medication for patients who require access to symptomatic relief during the course of a clinical study, for example when they are enrolled in a placebo-controlled study.
Risk Management Plan	Description of a pharmacovigilance programme for an approved product in the UK and EU, where risk management is an iterative process, throughout the time that a product is on the market, for assessing the risk:benefit of its use, ensuring that prescribers have the information and tools needed to use the product safely in patients, and making adjustments as needed to further improve the risk:benefit balance.
Safety Pharmacology	*In vitro* or animal pharmacology studies intended to assess the potential of a drug to have undesirable pharmacological effects in humans. These animal studies must be conducted to GLP.
Safety Signal	A concern about an excess of adverse events compared to what would be expected to be associated with a product's use. Signals can arise from a variety of sources, including postmarketing data, nonclinical studies, and events associated with other products in the same pharmacologic class. Even a single well-documented case report can be viewed as a signal. Signals need to be investigated to determine their potential causality, whether they represent a potential safety risk, and what other actions should be taken.
SBA	A Summary Basis of Approval is a publicly available summary of the review and evaluation conclusions of the US FDA regarding an approved product or indication. It is somewhat analogous to an EPAR.
Secondary Production Facility	The factory in which the active ingredient and excipients are combined on a production scale to produce a finished product that is subsequently packaged.
SEND	An electronic Standard for Exchange of Nonclinical Data to FDA which allows them to review individual animal data.
Serious Adverse Event	Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.
SmPC	The Summary of Product Characteristics is the UK, EMA or other EU regulatory agency-approved text that contains the most important information needed by a prescribing physician in order to make a decision on the suitability of a particular drug for a particular patient. The SmPC summarizes key efficacy, safety and risk:benefit information about the product. It is somewhat analogous to the PI in the US. UK-

Short Glossary of Terms (Version 1.3 of the MeduMaZe Drug Development & Approval Game; the most important ones are shown in BOLD type)

Acronym or Descriptive Term	Definition and Description
	approved SmPCs can be accessed from the Electronic Medicines Compendium or MHRA.
Sponsor	The sponsor takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization.
Spontaneous Adverse Events	The sponsor must promptly review all adverse drug experience information obtained or otherwise received from any source around the world, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers. The urgency for reporting this information to regulatory agencies depends on the severity of the event.
Starting Material	Starting materials are used in the production of small molecule drug substances. They are incorporated as a significant structural fragment into the active compound and they may be purchased from one or more suppliers, or produced by the sponsor. The starting material is generally considered to define the start of the synthetic route.
Toxicology Studies	The study of the toxic effects of substances. Studies are usually conducted in rodents and nonrodents (to GLP) to predict targets for human toxicity, dose response and potential reversibility. Early limit toxicity studies will involve single doses, while the recommended duration of repeated-dose toxicity studies is related to the duration, therapeutic indication, and scale of the proposed clinical trial.
Toxicokinetic	Toxicokinetics is the generation of pharmacokinetics data during a nonclinical toxicity study to assess systemic exposure of the drug to the animal. These data may be used in the interpretation of toxicology findings and their relevance to clinical safety issues.
User Fee	Any time a sponsor wants the MHRA, FDA, the EMA or other European regulatory agency to approve a new drug or biologic, it must submit a marketing application along with a user fee to support the review process.
Yellow Card scheme	As part of pharmacovigilance, the UK MHRA collects and monitors information on suspected safety concerns involving healthcare products, like side effects caused by a medicine, or adverse incidents involving medical devices, through the Yellow Card scheme.