Nutraceuticals World: Glossary of Terms

Absorption, Distribution, Metabolism and Excretion/Toxicology (ADME/T)
The objective of ADME/T testing is to measure what happens to a new compound in the human physiology. ADME/T tests are done during the pre-clinical stage of the Drug Discovery process and are a necessary provision of any clinical trial, prior to filing an IND.
ADME/T

Adverse Event (AE)
A negative experience encountered by an individual during the course of a clinical trial, which is associated with the drug/supplement. An AE can include previously undetected symptoms, or the exacerbation of a pre-existing condition. When an AE has been determined to be related to an investigational product, it is considered an Adverse Drug Reaction.
Adverse Event Reports (AERs)

Allocation Concealment
A method used to prevent selection bias by hiding the allocation sequence from those assigning participants to treatment groups, until the actual time of assignment. Allocation concealment prevents researchers from knowingly or unknowingly influencing which participants are assigned to a given treatment group. When executed well, the person(s) enrolling the subjects does not know in advance what treatment the next subject will be assigned to. Many published clinical trials lack a complete (or even any) description of the method of allocation concealment.
Assurance

Assay
A laboratory test or technique to identify and/or measure the amount of a particular substance in a sample, or for determining characteristics such as composition, purity, activity and weight. Used to determine whether compounds (drugs, chemicals, etc.) have the desired effect either in a living organism, outside an organism, or in an artificial environment.
Baseline

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

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

Bioassay
The determination of the biological activity of a drug by observing its effect on an organism (or organ) compared to a standard preparation.

Bioavailability
A measure of the uptake of an ingested substance by the body as assessed by its concentration in the blood. The rate and extent of its appearance in the blood are important determinants of bioavailability. Bioequivalence A scientific basis on which generic and brand name drugs are compared with one another. Drugs are bioequivalent if they enter circulation at the same rate when given in similar doses under similar conditions. Proof of bioequivalence is crucial for generic drugs.

Blind/Blinding
The process through which one or more parties to a clinical trial are unaware of the treatment assignments. In a single-blinded study, usually the subjects are unaware of the treatment assignments. In a double-blinded study, both the subjects and the investigators are unaware of the treatment assignments. Also, in a double-blinded study, the monitors and sometimes the data analysts are unaware. "Blinded" studies are conducted to prevent the unintentional biases that can affect subject data when treatment assignments are known. A randomized trial is "Blind" if the participant is not told which arm of the trial he is on. A clinical trial is "Blind" if participants are unaware on whether they are in the experimental or control arm of the study; also called masked. (See also Single-Blind Study and Double-Blind Study.)

Case Report Form
A record of pertinent information collected on each subject during a clinical trial, as outlined in the study protocol.

Centers For Disease Control and Prevention (CDC)
The Centers for Disease Control is charged with the tracking and investigation of public health trends and epidemics and publishes weekly reports on all deaths and diseases reported in the United States.

Clinical Investigation
A systematic study designed to evaluate a product (drug, device, dietary supplement or biologic) using human subjects in the treatment, prevention or diagnosis of a disease or condition, as determined by the product's benefits relative to its risks. Clinical investigations can only be conducted with the approval of the Food and Drug Administration (FDA).

Clinical Research
Study of drug, biologic, dietary supplement or device in human subjects with the intent to discover potential beneficial effects and/or determine its safety and efficacy. Also called clinical study and clinical investigation.

Clinical Research Associate (CRA)
Also known as a monitor, a CRA is an individual who oversees the progress and conduct of a clinical trial to ensure the scientific integrity of the data collected, and the protection of the rights, safety and well-being of human study subjects.

Code of Federal Regulations (CFR)
The Code of Federal Regulations (CFR) is a codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal government.

Cohort
In epidemiology, a group of individuals with some characteristics in common.

Contract Research Organization (CRO)
A company involved in performing clinical research on a contract basis for a pharmaceutical company, research organization, or other health organization. CROs are contracted to perform some or all of the duties by the sponsor for a clinical trial; examples include monitoring the trial, enrolling patients, performing statistical analysis and writing the protocols.

Cooperative Research and Development Agreement (CRADA)
A written agreement between a private company and a government agency to work together on a project. The collaborating partner agrees to provide funds, personnel, services, facilities, equipment or other resources needed to conduct a specific research or development effort, while the Federal government agrees to provide similar resources (but not funds) directly to the partner.

Control Group
A comparison group of study subjects who are not treated with the investigational agent. The subjects in this group may receive no therapy, a different therapy or a placebo.

Clinical Trial
A clinical trial is a research study to answer specific questions about vaccines, new therapies or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs, dietary supplements or treatments are both safe and effective. For a new pharmaceutical, the entire process typically takes 10 years and $200-250 million. The FDA approval process can take from six months to 10 years after the license application is filed; the average time now stands at about 30 months.

Crossover Trial
The same patient is being used in two different circumstances. This way there is little worry about a difference in genetics between patient populations. Some feel these studies are ideally suited for the nutraceuticals industry. Dietary Supplement Health & Education Act (DSHEA) In 1994, when the Dietary Supplement Health and Education Act (DSHEA) was passed, dietary supplements were categorized as food rather than drugs, based on the premise that they had a history of safe use and were therefore safe for use in the general population, unless proven otherwise. As with all foods, FDA's role is to evaluate the safety of supplements, independent of their benefits. While drugs are intended to treat or cure a disease, supplements are intended to reduce the risk of illness in a healthy population or to otherwise support health. For drugs the burden of proof of pre-market safety falls on the manufacturer, while the burden of proof of a product's post-market safety falls on the FDA for drugs and supplements alike. Little pre-market safety or efficacy data are available for supplements because many manufacturers rely on a presumed history of safe and effective use of these products.

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

Double-Masked Study
See Double-Blind Study.

DSHEA
See Dietary Supplement Health & Education Act.

Efficacy
Measures the power to produce, in a controlled setting such as a clinical trial, a stated effect typically attributable to a known physiologic phenomenon. It is important to derive measures of efficacy because, with appropriate statistical achievements, these data can approximate real-world effectiveness.

Endpoint
See Outcome Measure.

Epidemiology
The branch of medical science that deals with the study of incidence and distribution and control of a disease in a population.

FDA
See Food and Drug Administration.

Federal Food Drug and Cosmetic Act (FFDCA)
States only drugs, biologics and devices proven safe and effective can be marketed.

FFDCA
See Federal Food, Drug & Cosmetic Act.

Food and Drug Administration (FDA)
The U.S. Federal agency within the Department of Health and Human Services (HHS) charged with promoting and protecting public health by helping safe and effective products reach the market in a timely way and monitoring products for continued safety after they are in use. The agency was founded in 1938 to enforce the Federal Food, Drug and Cosmetic Act (FFDCA) and related Federal public health laws.

GCP
See Good Clinical Practice.

GLP
See Good Laboratory Practice.

GMP
See Good Manufacturing Practice.

Good Clinical Practice (GCP)
The international ethical and scientific quality standard for designing, conducting, monitoring, recording, auditing, analyzing and reporting studies. It ensures that the data reported is credible and accurate, and that subject's rights and confidentiality are protected.

Good Laboratory Practice (GLP)
A set of rules and criteria for a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported. The GLP principles have been developed to promote the quality and validity of data generated in the testing of chemicals in order to facilitate their recognition for purposes of assessment and other uses relating to the protection of human health and the environment.

Good Manufacturing Practice (GMP)
A set of principles and procedures which, when followed by manufacturers of dietary supplements and dietary ingredients, helps ensure that the products manufactured will be of the required quality. GMP is based on the premise that quality cannot be tested into a batch but must be built into each batch of product during all stages of manufacturing. (currently GMPs for dietary supplements are a proposed rule to be finalized by the end of 2003)

High Pressure Liquid Chromatography (HPLC)
A separation technique based on a solid stationary phase and a liquid mobile phase. Separations (into distinct bands) are achieved by partition, adsorption or ion-exchange processes, depending upon the type of stationary phase used. Each band is then profiled as the solvent flows through a UV detector, or by fluorescence, or refractive index (RI) detectors. Sometimes called high-performance liquid chromatography.

IND
See Investigational New Drug Application.

In-Licensing
Obtaining the right from another company to develop, produce and commercialize a particular compound. Inclusion/Exclusion Criteria The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are based on such factors as age, gender, the type and stage of a disease, previous treatment history and other medical

conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

Institutional Review Board (IRB)
An independent group of professionals designated to review and approve the clinical protocol, informed consent forms, study advertisements and patient brochures to ensure that a study is safe and effective for human participation. It is also the IRB's responsibility to ensure that the study adheres to a FDA's regulations.

Intent-To-Treat Analysis
A method of analyzing data from a randomized clinical trial wherein the individual outcomes observed are analyzed according to the group they were actually randomized to even if they never received the allocated treatment. This is a more rigorous statistical treatment of data sets that prevents the bias caused by subjects who dropout of a study and may also suggest non-adherence to the protocol/treatment.

Investigational New Drug Application (IND)
An application to the FDA to begin clinical trials of a new drug or biologic on humans. The IND gives the plan for the study and contains formulation, manufacturing and animal test result information.

Investigator
A medical professional, usually a physician but may also be a nurse, pharmacist or other healthcare professional, under whose direction an investigational drug is administered or dispensed. A principal investigator is responsible for the overall conduct of the clinical trial at his/her site.

In silico
In a computer model.

In vitro
Literally, "in glass." Performed in a test tube or other laboratory apparatus.

In vivo
In the living organism.

IRB
See Institutional Review Board.

Liquid Chromatography/Gas Chromatography (LC/GC)
Chromatography involves a sample (or sample extract) dissolved in a mobile phase (a gas, a liquid, or a supercritical fluid). The mobile phase is then forced through an immobile, immiscible stationary phase. The phases are chosen so that components of the sample have differing solubilities in each phase. As a result of these differences in solubilities, sample components will become separated from each other as they travel through the stationary phase. This process, in addition to separating components, also permits analysis. (See also High Pressure Liquid Chromatography.)

Mass Spectrometer
An analytical instrument that measures the mass of charged particles or ions. Works only on molecules that are charged or ionized; therefore, most biological samples must be subjected to conditions inside the spectrometer that cause the individual molecules to ionize.

Masked
The knowledge of intervention assignment. (See also Blind/Blinding.)

Medical Research
See Clinical Trial.

Medium
A substance containing nutrients needed for cell growth.

Methods Validation
Establishing, through documented evidence, a high degree of assurance that an analytical method will consistently yield results that accurately reflect the quality characteristics of the product tested.
National Center for Complementary and Alternative Medicine (NCCAM)
The National Center for Complementary and Alternative Medicine (NCCAM) is 1 of the 27 institutes and centers that make up the National Institutes of Health (NIH). The center's mission is to support rigorous research on complementary and alternative medicine (CAM), to train researchers in CAM and to disseminate information to the public and professionals on which CAM modalities work, which do not, and why. The center was established by Congress in 1998 and receives its funding from Congress.

National Institutes of Health (NIH)
Agency within the Department of Health and Human Services (HHS) that provides funding for research, conducts studies and funds multi-site national studies.

New Drug Application (NDA)
An application to FDA for a license to market a new drug in the U.S. Sponsor companies submit NDAs after completing clinical trials on a new drug.

Nutraceutical Research & Education Act (NREA)
This bill was introduced to Congress in 1999 by Congressman Frank Pallone. Its intention was to amend the Federal Food, Drug, and Cosmetic Act (FFDCA) to promote clinical research and development on dietary supplements and foods for their health benefits and to establish a new legal classification for dietary supplements and foods with health benefits, and for other purposes.

Off-Label Use
The use of a drug in a way neither approved by the FDA nor permitted to be put on its label and advertised as its intended purpose. Once a drug is approved by the FDA, physicians are free to prescribe it for any indication they see fit.

Office of Dietary Supplements (ODS)

The passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994 included authorization for the creation of the Office of Dietary Supplements (ODS) at the NIH and a Presidential Commission on Dietary Supplement Labels. The ODS was formally established on November 27, 1995 within the Office of Disease Prevention, Office of the Director, at the National Institutes of Health.The ODS supports research and disseminates research results in the area of dietary supplements. The ODS also provides advice to other Federal agencies regarding research results related to dietary supplements.

Open-Label Study
A study in which all parties, (patient, physician and study coordinator) are informed of the drug and dose being administered. In an open-label study, none of the participants are given placebos. These are usually conducted with Phase I & II studies.

Orange Book
An FDA-issued list of all approved prescription and OTC drug products. The list includes indications of "equivalency" for generic drugs, and also contains pertinent patent information. The Orange Book can be accessed online at www.fda.gov/cder/ob/default.htm.

Orphan Drugs
Drugs developed for rare diseases and conditions, which, in the U.S., affect fewer than 200,000 people or which, in the EU, affect five or fewer per 10,000 people. Because sales of orphan drugs are likely to be small compared to their development costs, pharmaceutical companies are awarded exclusive rights to market these medicines for a period of time (usually seven years) as an incentive to develop them and bring them to market.

Outcome Measure
An outcome variable of greatest interest/importance in a clinical trial. Differences between groups in outcome variables are believed to result from the different treatments. Data on secondary outcomes are used to evaluate additional effects of the intervention. Some researchers believe that if a treatment does not produce statistically significant differences in relation to a primary outcome measure then the secondary outcomes measures have far less clinical significance.

Out-Licensing
Selling the rights of a developed product(s) or potential compound to another firm for further development, production or marketing.

Parallel Study
A parallel study is a type of clinical trial in which the patients are usually randomized to different study groups and then followed at the same time. This design should be contrasted with crossover studies, in which the patients are treated in sequence.

Patent
A grant made by the government giving the creator of an invention the sole right to make, use and sell the invention for a set period of time.

Per-Protocol Analysis
A method of analyzing data from a randomized clinical trial wherein the individual outcomes observed are analyzed according to only those subjects that complete a trial as defined in the approved protocol. Typically this method of analysis yields more favorable interpretations than intent-to-treat analysis.

Pharmacodynamics
Study of the reactions between drugs and living structures. This covers a compound's pharmacologic effect on patients, including the study of uptake, movement, binding and interactions of agents at their tissue and cellular site(s) of action. (See also Pharmacology.)

Pharmacokinetics (PK)
The movements of drugs within biological systems, as affected by uptake, distribution, elimination and biotransformation. Abbreviated as PK. (See also Pharmacology.)

Pharmacology
The study of how drugs produce their effects. Pharmacology relies on knowledge of physiology, biochemistry, molecular biology and other scientific disciplines. (See also Pharmacodynamics and Pharmacokinetics.)

Phase I
Initial safety studies in humans. May include as few as 10 subjects, often in healthy volunteers, and includes PK, ADME/T and dose escalation studies to determine some side effects. Usually open label. Phase II Following initial safety (Phase I) testing, a drug is tested for efficacy, typically in blind, randomized trials, in which a control group receives a placebo. Phase II testing may last from several months to two years.

Phase II
Trials involve 100-300 subjects with the disease or condition of interest. Includes PK, dose ranging, safety and efficacy.

Phase III
Following Phase II testing, a drug is tested in a large-scale setting (several hundred to several thousand patients) to determine effectiveness, benefits and the range of possible adverse reactions. Most Phase III studies are randomized and double-blinded and typically last several years. Usually, two well-controlled studies are necessary to establish efficacy. Once Phase III trials are successfully completed, a pharmaceutical company can request FDA approval for marketing the drug, by filing a New Drug Application (See also NDA.). Phase IV Following FDA approval and marketing, companies may conduct further studies on their products. These post-approval studies have several objectives, including comparing the drug with other drugs already in the market, monitoring the drug's long-term effectiveness and determining additional potential uses for the drug.

Placebo
A mock treatment or drug that has no effect on the illness, given in a clinical trial to the control group to help differentiate the specific versus nonspecific effects of an experimental treatment.

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

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

Positive Control
A treatment that employs an agent(s) known to have a biological effect similar to that of the agent(s) being evaluated. In clinical trials this typically involves an innovator drug or biologic (e.g. sertraline, finasteride, tacrine or pravastatin). This is rarely employed in nutraceutical clinical trials but is a powerful comparator tool.

Pre-clinical Studies
Studies that test a drug or treatment on animals and in other nonhuman test systems. Safety information from such studies is used to support an Investigational New Drug (IND) application.

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

Protocol
A plan that sets guidelines for a trial and usually involves several different trial locations. A protocol is usually designed by the sponsor of a clinical trial.

Publication/Presentation Bias
The tendency or practice not to publish or present studies that do not show a statistically significant difference(s) between two or more groups. This is a not uncommon practice in both the pharmaceutical and nutraceutical industries.

QA See Quality Assurance.

QC See Quality Control.

Quality Assurance (QA)
The procedures established to ensure that a product is manufactured, or a clinical trial is performed, in compliance with the appropriate standards and regulatory requirements, and that the process or results are properly documented.

Quality Control (QC)
Checking or testing that specifications are met, or the regulatory process through which the industry measures actual quality performance, compares it with standards, and acts on the difference.

Randomization
A method of assignment whereby individuals have a known but not necessarily equal probability of being placed in a particular study or control group. Ideally it is performed via a computer generated number list or independent service that employs such a method.

Selection Bias
Error committed in creating treatment groups, wherein the groups differ in measured or unmeasured baseline characteristics because of the way in which participants were selected for the study or assigned to their study groups. The term is also used to describe the fact that the subjects are not representative of the population as a whole.

Single-Blind Study
A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study. (See also Blind/Blinding and Double-Blind Study.)

Single-Masked Study
See Single-Blind Study.

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

Subject
A subject is an individual who participates in a clinical trial. Usually these are diseased patients, except in Phase 1 studies.

Technology Transfer
The process of transferring discoveries made by basic research institutions, such as universities and government laboratories, to the commercial sector for development into useful products and services.

Validation
The establishment of documented evidence (for example, data derived from rigorous testing) that provides a high degree of assurance that a specific process or system will consistently yield a product meeting predetermined specifications and quality attributes