

Glossary

Clinical Trials Terminology

The following glossary of clinical trial terms is the second produced by the Glossary Group of CDISC. Version 2.0 is the latest CDISC Glossary as of the date of this publication. It consolidates terms from a number of primary sources, including ICH, FDA, SQA, the American Medical Association (AMA) Style Manual, HL7 and the HL7 Regulated Clinical Research and Information Management's (RCRIM) Protocol Representation Group, as well as the glossary published by *Applied Clinical Trials*. As did the first version, this second CDISC glossary includes terms that are specifically relevant to the CDISC standards and mission to develop standards to support the electronic acquisition, exchange, submission, and archiving of clinical trial data. It also includes terminology for paper-based processes where such terminology is relevant for eClinical trials.

A companion glossary of abbreviations, initialization and acronyms has also been compiled by CDISC.

Glossary terms have the following format and are organized alphabetically. Note, however, that the Glossary recognizes the recent practice of preceding certain terms with the letter "e" to denote that the term pertains to electronic or Web implementation. Such terms may appear twice in the glossary, once in alphabetical order under "e" and following the definition of the same term without the "e" prefix. The Glossary will also be posted on the CDISC Web site (www.cdisc.org) where comments are invited via the "Public Discussion Forum".

Each term in the Glossary has the following format:

- Term (abbreviation, initialization or acronym)
- Definition [Definition Source(s)]
- (Synonyms)
- NOTE: notes add usage conventions and relevant domain information to the definitions
- ("see also" statements)

absorption. The process by which medications reach the blood stream when administered other than intravenously, for example, through nasal membranes. See also *ADME (pharmacokinetics)*.

action letter. An official communication from FDA to an NDA sponsor announcing an agency decision. See also *approval letter, approvable letter, not-approvable letter*.

admission criteria. Basis for selecting target population for a clinical trial. Subjects must be screened to ensure that their characteristics match a list of admission criteria and that none of their characteristics match any single one of the exclusion criteria set up for the study. See also *inclusion criteria*.

adverse drug experience. See *adverse drug reaction*.

adverse drug reaction (ADR). In the preapproval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function. [CPMP/ICH/135/95] For further information, see the *ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited*

Reporting. See also *unexpected adverse drug reaction*. Synonyms: *adverse reaction, adverse drug reaction*.

adverse event (AE). Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. [CPMP/ICH/135/95] For further information, see the *ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting*. Synonyms: *side effect, adverse experience*. See also *serious adverse event, serious adverse experience*.

adverse experience. See *adverse event*.

adverse reaction. See *adverse drug reaction*.

algorithm. Step-by-step procedure for solving a mathematical problem; also used to describe step-by-step procedures for making a series of choices among alternative decisions to reach an outcome.

aliquot. A part that is a definite fraction of a whole, as in aliquot samples for laboratory testing or analysis.

alpha error. Size of the likelihood acceptable to the investigators that a relationship observed between 2 variables is due to chance the probability of a Type I error. See also *Type 1 error*.

American National Standards Institute (ANSI). Founded in 1918, ANSI itself does not develop standards. ANSI's roles include serving as the coordinator for U.S. voluntary standards efforts, acting as the approval body to recognize documents developed by other national organizations as American National Standards, acting as the U.S. representative in international and regional standards efforts, and serving as a clearinghouse for national and international standards development information. [HL7]

analyte. A substance being analyzed; in chromatography, a single component (compound) of a mixture.

applet. A small application, typically downloaded from a server.

application (computer). Software designed to fill specific needs of a user; for example, software for navigation, project management, or process control. *Synonyms:* *computer application, application software*.

application (regulatory). Application made to a health authority to market or license a new product.

application software. See *application*.

approvable letter. An official communication from FDA to an NDA sponsor that lists minor issues to be resolved before an approval can be issued.

approval (in relation to institutional review boards). The affirmative decision of the IRB that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the IRB, the institution, good clinical practice (GCP), and the applicable regulatory requirements. [ICH]

approval letter. An official communication from FDA to inform an NDA sponsor of an agency decision that allows commercial marketing of a product.

arm. A sequence of epochs (time intervals during which treatment is consistent), defining the course of participation for a subject in a trial. See also *epoch*.

audit (of a clinical trial). A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [ICH]

audit certificate. Document that certifies that an audit has taken place (at an investigative site, CRO, or clinical research department of a pharmaceutical company).

audit report. A written evaluation by the sponsor's auditor of the results of the audit. [ICH]

audit trail. Documentation that allows reconstruction of the course of events [ICH]. A secure, time stamped record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic study record. [FDA Guidance on Computerized Systems Used in Clinical Trials]

balanced study. Trial in which a particular type of subject is equally represented in each study group.

bandwidth. An indicator of the throughput (speed) of data flow on a transmission path; the width of the range of frequencies on which a transmission medium carries electronic signals. All digital and analog signals have a bandwidth.

baseline assessment. Assessment of subjects as they enter a trial and before they receive any treatment.

Bayesian approaches. Approaches to data analysis that provide a posterior probability distribution for some parameter (e.g. treatment effect), derived from the observed data and a prior probability distribution for the parameter. The posterior distribution is then used as the basis for statistical inference. [ICH E9]

Bayesian statistics. Statistical approach named for Thomas Bayes (1701–1761) that has among its features giving a subjective interpretation to probability, accepting the idea that it is possible to talk about the probability of hypotheses being true and of parameters having particular values.

beta error. Probability of showing no significant difference when a true difference exists; a false acceptance of the null hypothesis. See also *Type 2 error*.

between-subject variation. In a parallel trial design, differences between subjects are used to assess treatment differences.

bias (operational, statistical). The systematic tendency of any factors associated with the design, conduct, analysis, and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value. Bias introduced through deviations in conduct is referred to as operational bias. Other sources of bias (listed above) are referred to as statistical. [ICH E9]

bioanalytical assays. Methods for quantitative measurement of a drug, drug metabolites, or chemicals in biological fluids.

bioavailability. Rate and extent to which a drug is absorbed or is otherwise available to the treatment site in the body.

bioequivalence. Scientific basis on which generic and brand-name drugs are compared. To be considered bioequivalent, the bioavailability of two products must not differ significantly when the two products are given in studies at the same dosage under similar conditions.

biological marker. See *biomarker*.

biomarker. A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

biostatistics. Branch of statistics applied to the analysis of biological phenomena.

blind review. Checking and assessing data, during the period of time between trial completion (the last observation on the last subject) and breaking the blind, for the purpose of finalizing the planned analysis. [ICH E9]

blind study. One in which the subject, the investigator, or anyone assessing the outcome is unaware of the treatment assignment(s). Blinding is used to reduce the potential for bias. See also *blinding\masking*, *double-blind study*, *single-blind study*, *triple-blind study*.

blinded (masked) medications. Products that appear identical in size, shape, color, flavor, and other attributes to make it very difficult for subjects and investigators (or anyone assessing the outcome) to determine which medication is being administered.

blinding/masking. A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s). [ICH]

browser. Computer program that runs on the user's desktop computer and is used to navigate the World Wide Web. See also *Web browser*.

cache. Storage area on a computer's hard drive where the browser stores (for a limited time) Web pages and/or graphic elements.

carry-over effect. Effects of treatment that persist after treatment has been stopped, sometimes beyond the time of a medication's known biological activity.

case history. An adequate and accurate

record prepared and maintained by an investigator that records all observations and other data pertinent to the investigation on each individual administered the investigational drug (device or other therapy) or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study. [21 CFR 312.6b]

case record form. See *case report form*.

case report form (CRF). A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor for each trial subject [ICH]. A record of clinical study observations and other information that a study protocol designates must be completed for each subject. In common usage, CRF can refer to either a *CRF page*, which denotes a group of one or more *data items* linked together for collection and display, or a *casebook*, which includes the entire group of CRF pages on which a set of clinical study observations and other information can be or have been collected, or the information actually collected by completion of such CRF pages for a subject in a clinical study.

case report tabulations (CRT). In a paper submission, listings of data that may be organized by domain (type of data) or by subject. See also *eCRT*.

categorical data. Data evaluated by sorting values (for example, severe, moderate, and mild) into various categories.

causality assessment. An evaluation performed by a medical professional concerning the likelihood that a therapy or product under study caused or contributed to an adverse event.

Certified IRB Professional (CIP). Certification awarded to persons who satisfy the educational and employment requirements and pass an examination

conducted by the Applied Research Ethics National Association (ARENA), the membership division of Public Responsibility in Medicine and Research (PRIM&R).

clean database. A set of reviewed data in which errors have been resolved to meet QA requirements for error rate and in which measurements and other values are provided in acceptable units; database that is ready to be locked. See also *database lock*.

clean file. See *clean database*.

client. A program that makes a service request of another program (the server) that fulfills the request. Web browsers (such as Netscape Navigator and Microsoft Explorer) are clients that request HTML files from Web servers.

clinical clarification. A query resolution received from the sponsor staff (medical monitors, DSMB monitoring board, etc.). See also *self-evident change*.

clinical data. Data pertaining to the medical well-being or status of a patient or subject.

clinical efficacy. Power or capacity to produce a desired effect (i.e., appropriate pharmacological activity in a specified indication) in humans. [SQA]

clinical investigation brochure. See *investigator's brochure*.

clinical investigation. See *clinical trial*.

clinical pharmacology. Science that deals with the characteristics, effects, properties, reactions, and uses of drugs, particularly their therapeutic value in humans, including their toxicology, safety, pharmacodynamics, and pharmacokinetics (ADME).

clinical protocol. See *protocol*.

clinical research and development. The testing of a drug compound in humans primarily done to determine its safety and pharmacological effectiveness. Clinical development is done in phases, which progress from very tightly controlled dosing of small number of subjects to less tightly controlled studies involving large numbers of patients. [SQA]

clinical research associate (CRA). Person employed by a sponsor, or by a contract research organization acting on a sponsor's behalf, who monitors the progress of investigator sites participating in a clinical study. At some sites (primarily in academic settings), clinical research coordinators are called CRAs.

clinical research coordinator (CRC). Person who handles most of the administrative responsibilities of a clinical trial, acts as liaison between investigative site and sponsor, and reviews all data and records before a monitor's visit. *Synonyms: trial coordinator, study coordinator, research coordinator, clinical coordinator, research nurse, protocol nurse.*

clinical significance. Change in a subject's clinical condition regarded as important whether or not due to the test article. Some statistically significant changes (in blood tests, for example) have no clinical significance. The criterion or criteria for clinical significance should be stated in the protocol.

clinical study. See *clinical trial*.

clinical trial data. Data collected in the course of a clinical trial. See *clinical trial information*.

clinical trial exemption (CTX). A scheme that allows sponsors to apply for approval for each clinical study in turn, submitting supporting data to the Medicines Control Agency (MCA), which approves or rejects the application (generally within 35 working days). Approval means that the company is exempt from the requirement to hold a clinical trial certificate (CTC). (UK)

clinical trial information. Data collected in the course of a clinical trial or documentation related to the integrity or administration of that data. A superset of clinical trial data.

clinical trial materials. Complete set of supplies provided to an investigator by the trial sponsor.

clinical trial. A systematic study of a test article (treatment, drug or device) in one or more human subjects [21 CFR 50.3]. An investigation in human subjects intended to discover or verify the clinical,

pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy [ICH]. *NOTE: For the purposes of CDISC, this definition is extended to include medical devices and other investigational products regulated like pharmaceuticals. Synonyms: clinical study, clinical investigation. See also intervention.*

clinical trial/study report. A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analysis are fully integrated into a single report. [ICH] *For further information, see the the ICH Guideline for Structure and Content of Clinical Study Reports.*

coding. In clinical trials, the process of assigning data to categories for analysis. Adverse events, for example, may be coded using MedDRA. See also *acronym glossary*.

cohort. Group of subjects in a clinical trial followed up at regular, predetermined intervals. In epidemiology, a group of individuals with some characteristics in common.

cohort study. Study of a group of individuals, some of whom are exposed to a variable of interest, in which subjects are followed over time. Cohort studies can be prospective or retrospective. [AMA] See also *prospective study*.

Common Technical Document. A format agreed upon by ICH to organize applications to regulatory authorities for registration of pharmaceuticals for human use.

comparative study. One in which the investigative drug is compared against another product, either active drug or placebo.

comparator (product). An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical trial. [ICH]

Competent Authority (CA). The regulatory body charged with monitoring compliance with the national statutes and regulations of European Member States.

complete file. File for which all data cleaning is complete and database is ready for quality review and unblinding.

compliance (in relation to trials). Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements. [ICH]

computer application. See *application*.

confidentiality. Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a subject's identity. [ICH]

conformity assessment. The process by which compliance with the EMEA's Essential Requirements is assessed. See also *Notified Body*.

consent form (CF). Document used during the consent process that is the basis for explaining to potential subjects the risks and potential benefits of a study and the rights and responsibilities of the parties involved. *Synonym: informed consent form.*

consumer safety officer (CSO). FDA official who coordinates the review process of various applications.

content validity. The extent to which a variable (for example, a rating scale) measures what it is supposed to measure. [ICH E9]

contract. A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract. [ICH]

contract research organization (CRO). A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions. [ICH]

control group. The group of subjects in a controlled study that receives no treatment,

a standard treatment, or a placebo. FDA regulations recognize five controls that can be useful in particular circumstances, four concurrent (placebo, dose-comparison, no treatment, and active treatment) and one historical. [21 CFR 314.126]

control(s). A well-controlled study permits a comparison of subjects treated with the investigational drug with a suitable control population, so that the effect of the investigational drug can be determined and distinguished from other influences, such as spontaneous change, placebo effects, concomitant therapy, or observer expectations. [21 CFR 312.126]

controlled study. A study in which a test article is compared with a treatment that has known effects. The control group may receive no treatment, standard treatment, or placebo.

coordinating center. Headquarters for a multisite trial that collects all data.

coordinating committee. A committee that a sponsor may organize to coordinate the conduct of a multicenter trial. [ICH]

coordinating investigator. An investigator assigned the responsibility for the coordination of investigators at different centers participating in a multicenter trial. [ICH]

correlation. The relationship of one variable to another, not to be confused with causation.

CRF (paper). Case report form in which the data items on the CRF pages are linked by the physical properties of paper, for which data are captured manually and where any comments, notes, and signatures are also linked to those data items by writing or typescript on the paper CRF. See also *eCRF, case report form*.

crossover trial. In crossover trials, each subject receives both treatments being compared or the treatment and control. Such trials are used for patients who have a stable, usually chronic, condition during both treatment periods. Generally, both subjects and investigators are blinded to treatment assignment and sequence, and there is usually a washout period between phases. [SQA]

curriculum vitae (cv). Document that outlines a person's educational and professional history.

data. Representations of facts, concepts, or instructions in a manner suitable for communication, interpretation, or processing by humans or by automated means. [FDA] See also *information*.

data acquisition. Capture of data into a structured computerized format without a human-computer interface (from another automated or computerized source). *Contrast with data entry, electronic data capture.*

data and safety monitoring board (DSMB). Researchers, ideally independent of the trial data they monitor, who periodically review data from blinded, placebo-controlled trials. A DSMB can stop a trial if it finds toxicities or if treatment is proved beneficial. See also *independent data-monitoring committee*.

data clarification. Answer provided by an investigator in response to a query. The investigator supplies a new data point (for example, a systolic blood pressure value of 148) or confirms the errant data point (for example, the subject is truly 7 feet 4 inches tall).

data element. A named unit of data that, in some contexts, is considered indivisible and in other contexts may consist of data items (ISO). A named identifier of each of the entities and their attributes that are represented in a database. [FDA]

Data Encryption Standard (DES). A widely used method of data encryption using a private (secret) key that the U.S. government judged so difficult to break that it was restricted for export to other countries. Each message uses one of 72 quadrillion or more possible encryption keys that are chosen at random. The sender and receiver must both know and use the same private key. DES applies a 56-bit key to each 64-bit block of data.

data entry. Human input of data into a structured, computerized format using an interface such as a keyboard, pen-based tablet, or voice recognition. *Contrast with data acquisition, electronic data capture.*

data integrity verification. Process of binary file verification/no disk errors: print and check random pages from original submission and the magnetic disk copy; compare with the onscreen representation; perform a set of on-line searches manually and using the Verity search of the supplied indexes; analyze access logs will be analyzed with log analysis software.

data integrity. The degree to which a collection of data is complete, consistent, and accurate. [FDA/IEEE]

data interchange. Transfer of information between two or more parties that maintains the integrity of the contents of the data for the agreed purpose intended.

data item. A named component of a data element. Usually the smallest component (ANSI). See also *data model*. [FDA]

data management. Data management begins with the submission of the CRF to the sponsor and includes activities related to handling clinical study data, including database creation, data entry, review, coding, data editing, data QC, archiving and reporting of the database.

data management conventions. Documented procedure(s) for resolving self-evident changes. *Synonym: Self-evident conventions.*

data management personnel. Persons primarily responsible for database creation, data validation, integration, coding, and QC, archiving, and preparing data displays. [SQA]

data model. Unambiguous, formally stated, expression of items, the relationship among items, and the structure of the data in a certain problem area or context of use. A data model uses symbolic conventions agreed to represent content so that content does not lose its intended meaning when communicated.

data monitoring committee. See *independent data monitoring committee*.

data monitoring. Process by which case report forms are examined for completeness, consistency, and accuracy.

data quality. Validated quality is established by internal and external benchmarking,

quality control, and auditing systems and processes designed to ensure that trials are performed in compliance with FDA regulations and guidelines. See also *ALCOA*.

data security. Freedom from the risk of exposing data to accidental or malicious alteration or destruction; measures adopted to ensure data security. [FDA]

data validation. Process used to determine if data are inaccurate, incomplete, or unreasonable. The process may include format checks, completeness checks, check key tests, reasonableness checks, and limit checks [ISO]. Checking data for correctness and/or compliance with applicable standards, rules, and conventions. [FDA]

data verification. The process of ensuring that data at any point accurately represents the source data.

database lock. The point at which all clinical trial data has been reviewed, queries resolved, and issues addressed, and the

database can no longer be changed in any manner; a locked database is ready to undergo statistical analysis. *Synonym: database freeze.* See also *clean database*.

database. Data stored in computer form for retrieval, processing, and/or analysis.

Declaration of Helsinki. A set of recommendations or basic principles that guide medical doctors in the conduct of biomedical research involving human subjects. It was originally adopted by the 18th World Medical Assembly (Helsinki, Finland, 1964) and recently revised (52nd WMA General Assembly, Edinburgh, Scotland, October 2000).

demographic data. Characteristics of subjects or study populations, which include such information as age, sex, family history of the disease or condition for which they are being treated, and other characteristics relevant to the study in which they are participating.

derived variables. New variables created as

functions of existing variables or by applying mathematical operations.

development. Term used to describe the program for advancing a drug compound generally from the preclinical decision to concentrate on a single compound in a research program through its approval for marketing by the FDA and other regulatory agencies. [SQA] See also *drug development process*.

direct access. Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subject's identities and sponsor's proprietary information. [ICH]

discontinuation. The act of concluding participation in a trial for an enrolled subject. Various types of discontinuation occur: e.g., *dropout* (active discontinuation by a subject), *investigator-initiated* (e.g., for cause), *loss to follow-up* (subject ceased participation without notice or action by the subject), *sponsor-initiated discontinuation* (e.g., canceling the trial). *Synonym:* *termination (now considered nonstandard)*. See also: *withdrawal*. *NOTE:* Subject discontinuation does not necessarily imply exclusion of subject data from analysis. [HL7 Protocol Stds]

discrepancy. Data point that fails to pass a validation check. Discrepancies may be generated by computerized edit checks or observed/identified by the data reviewer as a result of manual data review.

distribution. In statistics, a group of ordered values; the frequencies or relative frequencies of all possible values of a characteristic [AMA]. In pharmacokinetics, the processes that control transfer of a drug from the site of measurement to its target and other tissues. See also *ADME*.

documentation. All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms)

that describe or record the methods, conduct and/or results of a trial, the factors affecting a trial, and the actions taken. [ICH]

domain name. The way a particular Web server is identified on the Internet. For example, *www.fda.gov* names the World Wide Web (www) server for the Food and Drug Administration, which is a government (gov) entity.

dosage form. The "delivery system" for a drug product, e.g., tablet, capsule, IV solution, topical cream. [SQA]

dosage regimen. The number of doses per given time period; the elapsed time between doses (for example, every six hours) or the time that the doses are to be given (for example, at 8 a.m. and 4 p.m. daily); and/or the amount of a medicine (the number of capsules, for example) to be given at each specific dosing time.

dosage. The amount of drug administered to a patient or test subject over the course of the clinical study; a regulated administration of individual doses. [AMA]

dose. The amount of drug administered to a patient or test subject at one time or the total quantity administered.

double-blind study. A study in which neither the subject nor the investigator nor the research team knows what treatment a subject is receiving.

double-dummy. A technique for retaining the blind when administering supplies in a clinical trial, when the two treatments cannot be made identical. Supplies are prepared for Treatment A (active and indistinguishable placebo) and for Treatment B (active and indistinguishable placebo). Subjects then take two sets of treatment; either A (active) and B (placebo), or A (placebo) and B (active). [ICH E9]

dropout. A subject in a clinical trial who for any reason fails to continue in the trial until the last visit required of him/her by the study protocol. [ICH E9]

drug. Article recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any

supplement to any of them; article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; article (other than food) intended to affect the structure or any function of the body; and articles intended for use as a component of any article specified above. Not a device or a component, part, or accessory of a device. [adapted from Food Drug & Cosmetic Act]

drug development process. The program for advancing a drug compound generally from the preclinical decision to recommend a single compound in a research program through its approval for marketing by the FDA and other regulatory agencies.

dynamic HTML. Collective term for a combination of new tags and options, style sheets, and programming that allows users to create Web pages in Hypertext Mark-up Language (HTML) that are more responsive to user interaction than previous versions of HTML.

eClinical trial record. Any data collected electronically in support of a clinical trial, including, but not limited to, the eCRF data. An electronic record [21 CFR 11] relevant to a clinical trial (e.g., medical history data, patient contact information, IVRS data, electronic patient diary data, electronic health record data relevant to clinical trials, clinical laboratory data). *NOTE:* This term can be used to denote a 'superset' of data, beyond what is required for the eCRF. An eClinical Trial record typically includes electronic data that support documentation of complete clinical cases and case histories. Such electronic records may include, or be limited to, the protocol-specific clinical trial data such as electronic source documents.

eClinical trial. Clinical trial in which primarily electronic processes are used to plan, collect (acquire), access, exchange and archive data required for conduct, management, analysis and reporting of the trial. Synonyms: eClinical study; eClinical investigation. See also *clinical trial*.

eCRF. Audible electronic record designed to record information required by the clinical trial protocol to be reported to the sponsor on each trial subject [FDA Guidance on Computerized Systems Used in Clinical

Trials]; a CRF in which related data items and their associated comments, notes, and signatures are linked electronically. *NOTE: eCRFs may include special display elements, electronic edit checks, and other special properties or functions and are used for both capture and display of the linked data.*

eCRT. CRTs provided in electronic format for eSubmissions (electronic regulatory submissions). *NOTE: According to current FDA guidance, eCRTs are datasets provided as SAS Transport files with accompanying documentation. They enable reviewers to analyze each dataset for each study. Each CRF domain should be provided as a single dataset, however additional datasets suitable for reproducing and confirming analyses may also be needed.*

edit check. A validation rule electronically programmed to run on data. *NOTE: edit checks commonly detect database data values outside of expected ranges or to identify missing data or dataset internal inconsistency.*

effect. An effect attributed to a treatment in a clinical trial. In most clinical trials, the treatment effect of interest is a comparison (or contrast) of two or more treatments. [ICH E9] *Synonym: treatment effect.*

effectiveness. The desired measure of a drug's influence on a disease or condition as demonstrated by substantial evidence from adequate and well-controlled investigations.

efficacy. The capacity of a drug or treatment to produce beneficial effects on the course or duration of a disease at the dose tested and against the illness for which it is designed.

electronic data capture (EDC). The process of collecting data into a permanent electronic form. *NOTE: "Permanent" in the context of these definitions implies that any changes made to the electronic data are recorded via an audit trail. See also data entry, data acquisition.*

eMedical record. An electronic record derived from a computerized system used primarily for delivering patient care in a clinical setting. *NOTE: eMedical records may serve as source documents, and such data could serve also as source data for clinical*

trials provided that the controls on the eMedical record system and the transfer of such data to the eClinical trial system were to fulfill the requirements of 21 CFR 11.

endpoint. An indicator or outcome measured in a subject or biological sample to assess the safety, efficacy, or other objective of a trial. Variable that pertains to the efficacy or safety evaluations of a trial. *NOTE: Not all endpoints are themselves assessments since certain endpoints might apply to populations or emerge from analysis of results. That is, endpoints might be facts about assessments (e.g., prolongation of survival). See also variable, surrogate marker.*

enroll. Admit a subject for participation in a clinical trial. Enrolled subjects are said to meet formal inclusion and exclusion criteria and are scheduled to participate in a trial in accordance with the protocol. *See also first subject in, target enrollment.*

enrollment. The act of enrolling one or more subjects to a clinical trial; the class of enrolled subjects in a clinical trial. Types of enrollment can be distinguished: *current enrollment: subjects actively participating in the trial as of the current date; cumulative enrollment: both current enrollment and any ever-enrolled subjects who have ended participation.*

epoch. An interval of time in the planned conduct of a study during which the treatment is consistent. *NOTE: There are no gaps between epochs in a trial; during execution of a trial, the planned epoch may serve as a label to associate captured data and information with that epoch. Synonyms: period, cycle, phase, stage. See also arm.*

equipoise. A state in which an investigator is uncertain about which arm of a clinical trial would be therapeutically superior for a patient. An investigator who has a treatment preference or finds out that one arm of a comparative trial offers a clinically therapeutic advantage should disclose this information to subjects participating in the trial.

equivalence trial. A trial with the primary objective of showing that the response to two or more treatments differs by an amount that is clinically unimportant. This

is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences. [ICH E9]

eSource data (electronic source data).

Source data captured initially into a permanent electronic record. [ICH] *NOTE: "Permanent" in the context of these definitions implies that any changes made to the electronic data are recorded via an audit trail. See also source data.*

essential documents. Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. [ICH]

ethics committee. See *institutional review board, independent ethics committee.*

European Agency for the Evaluation of Medicinal Products (EMA). The regulatory agency for the EU.

exclusion criteria. List of criteria in a protocol, any one of which excludes a potential subject from participation in a study. *Note: Exclusion and inclusion criteria define the study population.* [SQA] See also *inclusion criteria.*

excretion. The act or process of eliminating waste products from the body. See also *ADME.*

explanatory trial. Term used to describe a clinical study designed to demonstrate the efficacy of a product. See also *pragmatic trial.*

external consistency. The consistency of a procedure between sets of data.

File Transfer Protocol. A standard protocol for exchanging files between computers on the Internet. Used to transfer Web page files to the computer that acts as a server for everyone on the Internet. Also commonly used to download programs and other files to your computer from other servers. FTP is usually one of the programs that come with TCP/IP. See also *TCP/IP.*

final report. Complete, comprehensive description of a completed trial that describes the experimental materials and statistical design. It also presents and

evaluates the trial results and statistical analyses.

firewall. A set of related programs, located at a network gateway server, that protects a private computer network from users from other networks. Also the security policy that is used with the programs.

first subject in (FSI). The date and time the first subject is enrolled and randomized into a study. The subject will have met the inclusion/exclusion criteria to participate in the trial and have signed informed consent.

first subject screened. First subject that signs the informed consent form and is screened for potential enrollment and randomization into a study. At this time, the subject has not yet met the inclusion/exclusion criteria for the trial.

first-in-humans study. The first Phase 1 study in which the test product is administered to human beings.

first-in-man study. See *first-in-humans study.*

Food and Drug Administration (FDA). The United States regulatory authority charged with, among other responsibilities, granting IND and NDA approvals.

frequentist methods. Statistical methods, such as significance tests and confidence intervals, which can be interpreted in terms of the frequency of certain outcomes occurring in hypothetical repeated realizations of the same experimental situation. [ICH E9]

frozen file. Status of database when all data cleaning is completed, unblinding occurs, quality review of data is completed, all outstanding corrections have been addressed, and the database has been locked. See also *clean database.*

full analysis set. The set of subjects that is as close as possible to the ideal implied by the intention-to-treat principle. It is derived from the set of all randomized subjects by minimal and justified elimination of subjects. [ICH E9]

gas chromatography (GC). A process by which the components of a mix are separated from one another by volatilizing the sample into a carrier gas stream and passing the gas through a column containing a substance that

selectively retains (adsorbs) and releases the volatile constituents.

gender. Subject self-identification as a male or female person [IOM]. Gender signifies an individual's personal, legal, and social status without reference to genetic sex, which is an objective biological fact. [AMA]

generalizability, generalization. The extent to which the findings of a clinical trial can be reliably extrapolated from the subjects who participated in the trial to a broader patient population and a broader range of clinical settings. [ICH E9]

global assessment variable. A single variable, usually a scale of ordered categorical ratings, which integrates objective variables and the investigator's overall impression about the state or change in state of a subject. [ICH E9]

glossary. A collection of specialized terms with their meanings.

good clinical practice (GCP). A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. [ICH] *NOTE: for Guidance on Good Clinical Practice see CPMP/ICH/135/95; Declaration of Helsinki; 21 CFR 50, 21 CFR 54, 21 CFR 56, and 21 CFR 312.*

good clinical research practice (GCRP). Term sometimes used to describe GCP. See *good clinical practice.*

Harmonized Standard. A European Norm (EN) that has been accepted by all Member States and has been published in the *Official Journal of the European Communities* (OJEC).

Health Level 7 (HL7) messaging. An application protocol for electronic data exchange in health care environments. The HL7 protocol is a collection of standard formats that specify the implementation of interfaces between computer applications from different vendors. This communication protocol allows health care institutions to exchange key sets of data between different application systems. [HL7]

healthy volunteer. A healthy person who

agrees to participate in a clinical trial for reasons other than medical and receives no direct health benefit from participating. See *also human subject*.

heterologous. Consisting of different elements, or of elements in differing proportions.

human subject. A human subject, as defined in 21 CFR 50.3, is an "individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient."
Synonym: subject/trial subject.

Huriet Law. France's regulations covering the initiation and conduct of clinical trials.

HyperText Markup Language (HTML). A set of codes that describes the way type, graphics, and other elements are displayed on a Web page.

hypertext. Links in a document that permit you to jump immediately to another document. In most Web browsers links are displayed as colored, underlined text.

impartial witness. A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject. [ICH]

inclusion criteria. The criteria in a protocol that prospective subjects must meet to be eligible for participation in a study. *NOTE: Exclusion and inclusion criteria define the study population. See also exclusion criteria.*

independent data monitoring committee (IDMC). An independent data-monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial. *Also called data and safety monitoring board, monitoring committee, data monitoring committee.* [CH E9]

independent ethics committee (IEC). An

independent body (a review board or a committee, institutional, regional, national, or supranational) constituted of medical/scientific professionals and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial and to provide public assurance of that protection by, among other things, reviewing and approving/providing favorable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to independent ethics committees may differ among countries, but should allow the independent ethics committee to act in agreement with GCP as described in the ICH guideline. [ICH] (*See also institutional review board.*)

indication. A health problem or disease that is identified as likely to be benefited by a therapy being studied in clinical trials. Where such a benefit has been established and approved by regulatory authorities, the therapy is said to be approved for such an indication.

informed consent. A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent precedes enrollment and is documented by means of a written, signed, and dated consent form. [ICH] *NOTE: Under 21 CFR 50.20, no informed consent may include any "language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence."*

inspection. The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments

deemed appropriate by the regulatory authority(ies). [ICH] *See also audit.*

institution (medical). Any public or private entity or agency or medical or dental facility where clinical trials are conducted. [ICH]

institutional review board (IRB). An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. [ICH] *Other names for such bodies include independent review board, independent ethics committee, committee for the protection of human subjects.*

intention-to-treat. The principle that asserts that the effect of a treatment policy can be best assessed by evaluating on the basis of the intention to treat a subject (i.e., the planned treatment regimen) rather than the actual treatment given. It has the consequence that subjects allocated to a treatment group should be followed up, assessed, and analyzed as members of that group irrespective of their compliance to the planned course of treatment. [ICH E9] *Synonym: Intent-to-treat.*

interaction (qualitative and quantitative). The situation in which a treatment contrast (e.g., difference between investigational product and control) is dependent on another factor (for example, the centre). A quantitative interaction refers to the case where the magnitude of the contrast differs at the different levels of the factor; for a qualitative interaction, the direction of the contrast differs for at least one level of the factor. [ICH E9]

interactivity. Interactions in cyberspace with other people, information, and computers. Examples of interactivity include sending an e-mail message and filling out an *Applied Clinical Trials* subscription form at www.superfill.com/subscribe/apct.htm

interim analysis. Any planned analysis intended to compare treatment arms with respect to efficacy or safety at any time

prior to the formal completion of a trial, determined as part of the study protocol prior to subject enrollment. [ICH E9]

interim clinical trial/study report. A report of intermediate results and their evaluation based on planned analyses performed during the course of a trial. [ICH]

internal consistency. A property of data that does not contradict itself.

Internet service provider (ISP). A company that provides access to the Internet for individuals and organizations. ISPs range in size from small local services to huge national providers, like Netcom and ComCast, and international full-service providers like America Online (AOL).

Internet. A global system of computer networks that provides the infrastructure for e-mail, the World Wide Web, and other online activities.

inter-rater reliability. The property of scales yielding equivalent results when used by different raters on different occasions. [ICH E9]

intervention. The drug, device, therapy or process under investigation in a clinical trial which has an effect on outcome of interest in a study: e.g., quality of life, efficacy, safety, pharmacoeconomics.

investigational product. A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. [ICH] *CDISC includes test articles in its definition of investigational products.*

investigator. A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. [ICH]. 21 CFR 50.3 expands on the ICH definition by stating that an investigator is the individual "under whose immediate direction the test article is administered or dispensed to, or

used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team." *See also sponsor-investigator.*

investigator/institution. An expression meaning "the investigator and/or institution, where required by the applicable regulatory requirements." [ICH]

investigator's brochure. A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects. [ICH]

item. An individual clinical data element, such as a single systolic blood pressure reading. Items are collected together into item groups. *See also data item.*

labeling. Description of the drug and summary of use, safety, and effectiveness that must be approved by FDA. [SQA]

last subject in (LSI). Date and time the last subject to participate in a clinical trial is enrolled. The subject will have met the inclusion/exclusion criteria to participate in the trial and have signed informed consent. *See also enroll.*

last subject out/complete (LSO/LSC). Last subject to complete a trial. *See also completion, last subject data collected.*

legally acceptable representative. An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial. [ICH]

Leiter der klinischen Prüfung. Under the German Drug Law, the physician who is head of the clinical investigation.

life-threatening adverse event/experience. Any adverse event/experience that, in the view of the investigator, places a subject at immediate risk of death. [SQA]

longitudinal study. Investigation in which data are collected from a number of subjects over a long period of time (a well-known example is the Framingham Study).

marketing support trials. Studies to assess

not only safety and efficacy on large patient populations, but also quality-of-life impact and cost-effectiveness. Many market support trial outcomes are used for additional indications of already approved drugs, publications and promotion purposes.

masking. See *blinding/masking*.

matched-pair design. A type of parallel trial design in which investigators identify pairs of subjects who are “identical” with respect to relevant factors, then randomize them so that one receives Treatment A and the other Treatment B. See also *pairing*.

matching. See *pairing*.

mean. The sum of the values of all observations or data points divided by the number of observations, an arithmetical average.

median. The middle value in a data set; that is, just as many values are greater than the median and lower than the median value. (With an even number of values, the conventional median is halfway between the two middle values.)

medical monitor. A sponsor representative who has medical authority for the evaluation of the safety aspects of a clinical trial.

Medicines Control Agency (MCA). The United Kingdom regulatory authority that approves or rejects CTX/CTC and PL applications.

mega-trials. Massive randomized clinical trials that test the advantages of marginally effective experimental drugs by enrolling 10,000 or more subjects. *Synonym: large-sample trials.*

Memorandum of Understanding (MOU). An MOU between FDA and a regulatory agency in another country allows mutual recognition of inspections.

meta-analysis. A statistical process for pooling data from many clinical trials and summarizing it through formal statistical means. *Also called overview.*

metabolism. The sum of the processes by

which a substance is handled in the living body. See also *ADME*.

metadata. Data that describes other data.

mode. The most frequently occurring value in a data set.

modem. From modulator/demodulator; a device that converts the digital data into analog data that can be transmitted via telephone or cable lines used for communications.

monitor. Person employed by the sponsor or CRO who is responsible for determining that a trial is being conducted in accordance with the protocol. A monitor's duties may include, but are not limited to, helping to plan and initiate a trial, assessing the conduct of trials, and assisting in data analysis, interpretation, and extrapolation. Monitors work with the clinical research coordinator to check all data and documentation from the trial. See also *clinical research associate*.

monitoring. The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [ICH]

monitoring committee. See *independent data-monitoring committee*.

monitoring report. A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOPs. [ICH]

monitoring visit. A visit to a study site to review the progress of a clinical study and to ensure protocol adherence, accuracy of data, safety of subjects, and compliance with regulatory requirements and good clinical practice guidelines. [SQA]

multicenter study. See *multicenter trial*.

multicenter trial. A clinical trial conducted according to a single protocol but at more

than one site, and therefore, carried out by more than one investigator. [ICH] *Synonym: multicenter study.*

New Drug Application (NDA). An application to FDA for a license to market a new drug in the United States.

n-of-1 study. A trial in which an individual subject is administered a treatment repeatedly over a number of episodes to establish the treatment's effect in that person, often with experimental and control treatments randomized.

nonclinical study. Biomedical studies not performed on human subjects. [ICH]

not-approvable letter. An official communication from FDA to inform an NDA sponsor that the important deficiencies described therein preclude approval unless corrected.

Notified Body (NB). A private institution charged by the Competent Authority with verifying compliance of medical devices (not drugs) with the applicable Essential Requirements stated in the Medical Device Directive. This process, called Conformity Assessment, has EU-wide validity once completed by the NB.

null hypothesis. A null hypothesis (for example, "subjects will experience no change in blood pressure as a result of administration of the test product") is used to rule out every possibility except the one the researcher is trying to prove, an assumption about a research population that may or may not be rejected as a result of testing. Used because most statistical methods are less able to prove something true than to provide strong evidence that it is false. The assertion that no true association or difference in the study outcome or comparison of interest between comparison groups exists in the larger population from which the study samples are obtained. *See also research hypothesis.*

Nuremberg Code. Code of ethics for conducting human medical research set forth in 1947.

objective measurement. A measurement that cannot be influenced by investigator bias; for example, blood glucose levels or ECG tracings.

open study. A trial in which subjects and investigators know which product each subject is receiving; opposite of a blinded or double-blind study.

open-label study. *See also open study.*

opinion (in relation to independent ethics committee). The judgment and/or the advice provided by an independent ethics committee. [ICH]

original medical record. *See source documents.*

outcome (variable). *See variable, endpoint.*

outcomes research. *See pharmacoeconomics.*

overview. *See meta-analysis.*

p value. The lowest level of significance at which a given null hypothesis can be rejected; that is, the probability of observing a result as extreme or more extreme than that observed if the null hypothesis is true. *See also statistical significance.*

pairing. A method by which subjects are selected so that two subjects with similar characteristics (for example, weight, smoking habits) are assigned to a set, but one receives Treatment A and the other receives Treatment B. *See also matched-pair design*

parallel trial. Subjects are randomized to one of two differing treatment groups (usually investigational product and placebo) and usually receive the assigned treatment during the entire trial. *Synonyms: parallel group trial, parallel design trial.*

parameter. A constant in a model, or a constant that wholly or partially characterizes a function of probability distribution (mathematics and statistics). In clinical research the term is often linked to statistical conventions and is a numeric characteristic of a population. Thus the term is narrower than variable.

patient. Person under a physician's care for a particular disease or condition. *See also subject/trial subject, healthy volunteer.*

patient file. Contains demographic, medical, and treatment information about a patient

or subject. It may be paper-based or a mixture of computer and paper records.

period effect. Designated period during the course of a trial in which subjects are observed and no treatment is administered.

pharmacodynamics (PD). Branch of pharmacology that studies reactions between drugs and living structures, including the processes of bodily responses to pharmacological, biochemical, physiological, and therapeutic effects.

pharmacoeconomics. Branch of economics that applies cost-benefit, cost-utility, cost-minimization, and cost-effectiveness analyses to compare the economics of different pharmaceutical products or to compare drug therapy to other treatments.

pharmacogenetics. Study of the way drugs interact with genetic makeup or the genetic response to a drug.

pharmacogenomics. Science that examines inherited variations in genes that dictate drug response and explores the ways such variations can be used to predict whether a person will have a good response to a drug, a bad response to a drug, or no response at all.

pharmacokinetics (PK). Study of the processes of bodily absorption, distribution, metabolism, and excretion (ADME) of compounds and medicines.

pharmacology. Science that deals with the characteristics, effects, and uses of drugs and their interactions with living organisms.

pharmacovigilance. Term used for adverse event monitoring and reporting in some countries.

pharmacogenetic test. An assay intended to study interindividual variations in DNA sequence related to drug absorption and disposition or drug action.

pharmacogenomic test. An assay intended to study interindividual variations in whole-genome or candidate gene maps, biomarkers, and alterations in gene expression or inactivation that may be correlated with pharmacological function and therapeutic response.

phases of clinical trials. Clinical trials are generally categorized into four (sometimes five) phases described below. An investigational medicine or product may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases.

Phase 1. The initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80. Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. [FDA]

Phase 2. Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications 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 typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects. [FDA]

Phase 3. Studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundred to several

thousand subjects. [FDA] *NOTE: Phase 3b studies are a sub category of Phase 3 trials near the time of approval to elicit additional findings.*

Phase 4. Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain postmarketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time. [FDA]

Phase 5 studies. Postmarketing surveillance is sometimes referred to as Phase 5.

placebo. A pharmaceutical preparation that contains no active agent. In blinded studies, it is generally made to look just like the active product.

population. Any finite or infinite collection of subjects from which a sample is drawn for a study to obtain estimates for values that would be obtained if the entire population were sampled. [AMA]

postmarketing surveillance. Ongoing safety monitoring of marketed drugs. *See Phase 4 studies, Phase 5 studies.*

pragmatic trial. Term used to describe a clinical study designed to examine the benefits of a product under real world conditions.

preclinical studies. Animal studies that support Phase 1 safety and tolerance studies and must comply with good laboratory practice (GLP). Data about a drug's activities and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical studies or trials). Because many animals have much shorter life spans than humans, preclinical studies can provide valuable information about a drug's possible toxic effects over an animal's life cycle and on its offspring.

primary variable. An outcome variable of interest in the trial. Differences in the outcome variable(s) between groups of

subjects are believed to be the result of the group-specific interventions. *See also outcome, endpoint.*

prospective study. Investigation in which a group of subjects is recruited and monitored in accordance with criteria described in a protocol.

protocol. A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term *protocol* refers to protocol and protocol amendments. [ICH]

protocol amendment. A written description of a change(s) to or formal clarification of a protocol. [ICH]

protocol approval. This marks completion of protocol development. The signature of the last reviewer on the protocol approval form has been obtained and signifies that all reviewer changes to the protocol have been incorporated.

qualitative variable. One that cannot be measured on a continuum and represented in quantitative relation to a scale (race or sex, for example). Data that fit into discrete categories according to their attributes.

quality assurance (QA). All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with good clinical practice (GCP) and the applicable regulatory requirement(s). [ICH]

quality control (QC). The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled. [ICH]

quantitative variable. One that can be measured (blood pressure, for example) and reported numerically, such as continuous data or counts.

query. Request from a sponsor or sponsor's representative to an investigator to resolve an error or inconsistency discovered during

data review. Request for clarification on a data item collected for a clinical trial.

query management. Ongoing process of data review, discrepancy generation, and resolving errors and inconsistencies that arise in the entry and transcription of clinical trial data.

query resolution. The closure of a query based on information contained in a data clarification

random allocation. Assignment of subjects to treatment (or control) groups in an unpredictable way. Assignment sequences are concealed, but available for disclosure in the event a subject has an adverse experience.

random number table. Table of numbers with no apparent pattern used in the selection of random samples for clinical trials.

random sample. Members of a population selected by a method designed to ensure that each person in the target group has an equal chance of selection.

randomization. The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. [ICH]

raw data. Researcher's records of subjects/patients, such as medical charts, hospital records, X-rays, and attending physician's notes. These records may or may not accompany an application to a Regulatory Authority, but must be kept in the researcher's file. [SQA/CDISC]

recruitment (investigators). Process used by sponsors to select investigators for a clinical study.

recruitment (subjects). Process used by investigators to enroll appropriate subjects (those selected on the basis of the protocol's inclusion and exclusion criteria) into a clinical study.

recruitment period. Time period during which subjects are or are planned to be enrolled in a clinical trial.

recruitment target. Number of subjects that

must be recruited as candidates for enrollment into a study to meet the requirements of the protocol. In multicenter studies, each investigator has a recruitment target.

regulatory authorities. Bodies having the power to regulate. In the ICH GCP guideline the term includes the authorities that review submitted clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities. [ICH] *Synonym: regulatory agencies.*

replacement. The act of enrolling a clinical trial subject to compensate for the withdrawal of another.

representative. See *legally acceptable representative.*

research hypothesis. The research hypothesis is the conclusion a study sets out to support (or disprove); for example, "blood pressure will be lowered by [specific endpoint] in subjects who receive the test product." See also *null hypothesis.*

result synopsis. The brief report prepared by biostatisticians summarizing primary (and secondary) efficacy results and key demographic information.

retrospective. Entry of clinical trial data is retrospective when it is recalled from memory rather than accomplished contemporaneously in real-time. Such retrospective entry is subject to "recall bias", which includes various differences that have been documented in psychological research between contemporaneous self-reported assessments and those that rely on memory.

risk. In clinical trials, the probability of harm or discomfort for subjects. Acceptable risk differs depending on the condition for which a product is being tested. A product for sore throat, for example, will be expected to have a low incidence of side effects. However, unpleasant side effects may be an acceptable risk when testing a promising treatment for a life-threatening illness.

safety. Relative freedom from harm. In clinical trials, this refers to an absence of harmful side effects resulting from use of

the product and may be assessed by laboratory testing of biological samples, special tests and procedures, psychiatric evaluation, and/or physical examination of subjects.

safety and tolerability. The safety of a medical product concerns the medical risk to the subject, usually assessed in a clinical trial by laboratory tests (including clinical chemistry and hematology), vital signs, clinical adverse events (diseases, signs and symptoms), and other special safety tests (e.g., ECGs, ophthalmology). The tolerability of the medical product represents the degree to which overt adverse effects can be tolerated by the subject. [ICH E9]

sample size. The number of subjects in a clinical trial; number of subjects required for primary analysis. Subset of a larger population, selected for investigation to draw conclusions or make estimates about the larger population.

sample size adjustment. An interim check conducted on blinded data to validate the sample size calculations or re-evaluate the sample size.

screen/screening (of substances). Screening is the process by which substances are evaluated in a battery of tests or assays (screens) designed to detect a specific biological property or activity. It can be conducted on a random basis in which substances are tested without any preselection criteria or on a targeted basis in which information on a substance with known activity and structure is used as a basis for selecting other similar substances on which to run the battery of tests. [SQA]

screening (of potential subjects). Active consideration of potential subjects for enrollment in a trial. *Screening failures* are potential subjects who did not meet one or more of the inclusion criteria (screens) required to be eligible to participate.

screening (of sites). Determining the suitability of an investigative site and personnel to participate in a clinical trial.

screening trials. Trials that test the best way to detect certain diseases or health conditions.

script. A program or a sequence of instructions that are interpreted or carried out by another program.

search engine. An online service that compares your search criteria with its database of information about the Internet and displays the results.

secondary variable. The primary outcome is the outcome of greatest importance. Data on secondary outcomes are used to evaluate additional effects of the intervention.

self-evident change. A data discrepancy that can be easily and obviously resolved on the basis of existing information on the CRF, e.g., obvious spelling errors or the patient is male and a date of last pregnancy is provided.

serious adverse event (SAE) or serious adverse drug reaction (serious ADR). Any untoward medical occurrence that at any dose: results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. [ICH] See also *adverse experience*.

serious adverse experience. Any experience that suggests a significant hazard, contraindication, side effect or precaution. [Nordic Guidelines for Good Clinical Trial Practice] See also *serious adverse event*.

server. A computer program that provides services to other computer programs in the same or other computers. See also *Web server*.

side effects. Any undesired actions or effects of a drug or treatment. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental drugs must be evaluated for both immediate and long-term side effects. See also *adverse reaction*.

single-blind study. A study in which one party, either the investigator or the subject, does not know which medication or placebo is administered to the subject; also called single-masked study. See also *blind and double-blind study*.

single-masked study. See *single-blind study*.

software. Computer programs, procedures, rules, and any associated documentation pertaining to the operation of a system.

source data. All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). [ICH]

source documents. Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial). [ICH]

sponsor. An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial. [ICH] A corporation or agency whose employees conduct the investigation is considered a sponsor and the employees are considered investigators. [21 CFR 50.3]

sponsor-investigator. An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator [ICH]. Under FDA regulations, the term does not include any person other than an individual, e.g., corporation or agency. [21 CFR 50.3f]

standard deviation. Indicator of the relative variability of a variable around its mean; the square root of the variance.

standard of care. Treatment regimen or medical management based on state-of-the-art patient care.

standard operating procedures (SOPs). Detailed, written instructions to achieve uniformity of the performance of a specific function. [ICH]

standard treatment. A treatment currently in wide use and approved by the FDA or other health authority, considered to be effective in the treatment of a specific disease or condition.

statistical analysis plan. A statistical analysis plan is a document that contains a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and includes detailed procedures for executing the statistical analysis of the primary and secondary variables and other data. [ICH E9]

statistical significance. State that applies when a hypothesis is rejected. Whether or not a given result is significant depends on the significance level adopted. For example, one may say "significant at the 5% level". This implies that a level of significance has been applied such that when the null hypothesis is true there is only a 1 in 20 chance of rejecting it or that the observed result has led to rejection of the null hypothesis.

stochastic. Involving a random variable; involving chance or probability.

stopping rules. A statistical criterion that, when met by the accumulating data, indicates that the trial can or should be stopped early to avoid putting participants at risk unnecessarily or because the intervention effect is so great that further data collection is unnecessary.

study coordinator. See *clinical research coordinator*.

study design. Plan for the precise procedure to be followed in a clinical trial, including planned and actual timing of events, choice of control group, method of allocating treatments, blinding methods; it assigns a subject to pass through one or more epochs in the course of a trial. Specific design elements, e.g., crossover, parallel; dose-escalation.

study protocol. See *protocol*.

study. See *clinical trial*.

sub-investigator. Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). [ICH] See also *investigator*.

subject identification code. A unique identifier assigned by the investigator to each trial subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial-related data. [ICH]

subject/trial subject. An individual who participates in a clinical trial, either as recipient of the investigational product(s) or as a control. [ICH] See also *healthy volunteer, human subject*.

superiority trial. A trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control). [ICH E9]

surrogate marker. A measurement of a drug's biological activity that substitutes for a clinical endpoint such as death or pain relief.

surrogate variable. A variable that provides an indirect measurement of effect in situations where direct measurement of clinical effect is not feasible or practical. [ICH E9]

system. People, machines, software, applications and/or methods organized to accomplish a set of specific functions or objectives. [FDA / ANSI]

target enrollment. The number of subjects in a class or group (including the total for the entire trial) intended to be enrolled in a trial to reach the planned sample size. Target enrollments are set so that statistical and scientific objectives of a trial will have a likelihood of being met as determined by agreement, algorithm or other specified process.

technology provider. Person, company, or other entity who develops, produces, and

sells software applications and/or hardware for use in conducting clinical trials and/or in analyzing clinical trial data and or submitting clinical trial information for regulatory approval. *Synonym: vendor*.

termination (of subject). Now considered nonstandard. See *discontinuation*.

transcription. Process of transforming dictated or otherwise documented information into an electronic format. [HL7]

treatment effect. An effect attributed to a treatment in a clinical trial. In most clinical trials the treatment effect of interest is a comparison (or contrast) of two or more treatments. [ICH E9]

treatment-emergent adverse event. An event that emerges during treatment, having been absent pretreatment, or worsens relative to the pretreatment state. [ICH E9]

trial coordinator. See *clinical research coordinator*.

trial site. The location(s) where trial-related activities are actually conducted. [ICH]

trial statistician. A statistician who has a combination of education/training and experience sufficient to implement the principles in the ICH E9 guidance and who is responsible for the statistical aspects of the trial. [ICH E9]

triple-blind study. A study in which knowledge of the treatment assignment(s) is concealed from the people who organize and analyze the data of a study as well as from subjects and investigators.

t-test. A statistical test used to compare the means of two groups of test data.

Type 1 (or Type I) error. Error made when a null hypothesis is rejected but is actually true. *Synonym: false positive*.

Type 2 (or Type II) error. Error made when an alternative hypothesis is rejected when it is actually true. *Synonym: false negative*.

Type 3 (or Type III) error. Some statisticians use this designation for an error made when calling the less effective treatment the more effective one.

unblinding. Identification of the treatment code of a subject or grouped results in studies where the treatment assignment is unknown to the subject and investigators.

unequal randomization. A technique used to allocate subjects into groups at a differential rate; for example, three subjects may be assigned to a treatment group for every one assigned to the control group. See also *balanced study*.

unexpected adverse drug reaction. An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., investigator's brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product). [ICH] See also *adverse drug reaction*.

uniform resource locator (URL). Address of a Web page—actmagazine.com, for example.

validation of data. Procedure carried out to ensure that the data contained in the final clinical trial report match original observations.

validity. The accuracy of the relationship between two or more variables.

variable. Any quantity that varies; any attribute, phenomenon, or event that can have different qualitative or quantitative values. Usually a form of metadata goes with the variable, a variable definition describes what is varying, and the variable has a value. *NOTE: In the context of a protocol, variables pertain to the study. Variable is an enveloping term that includes specific subtypes used in clinical research. "Study variable" is a term used in trial design to denote a characteristic to be captured on the CRF. An "assessment" is a study variable pertaining to the status of a subject. Assessments are usually measured at a certain time, and usually are not compounded significantly by combining several simultaneous measurements to form a derived assessment (e.g. BMI) or a result of statistical analysis. An "endpoint" is a variable that pertains to the trial objectives. Not all endpoints are themselves assessments since certain endpoints might apply to populations or emerge from analysis of results. That is,*

Ethics Committees

Bodies convened to protect human clinical research subjects work under a variety of other names. For convenience and consistency, *Applied Clinical Trials* generally uses the terms *institutional review board* and *ethics committee*. Other names and abbreviations for such bodies are shown below.

CCI committee on clinical investigations

CCPPRB Comité Consultative pour la Protection des Personnes dans les Recherches Biomédicales (France)

CHR committee on human research

CPPHS committee for the protection of human subjects

CRB central review board

EAB ethical advisory board

EC ethics committee

HEX human experimentation committee

HSRC human subjects review committee

IEC independent ethics committee

IRB independent review board; institutional review board

LREC local research ethics committees (UK)

MREC multicentre research ethics committees (UK)

NIRB noninstitutional review board

NRB noninstitutional review board, also known as an independent review board

REB research ethics board (Canada)

endpoints might be facts about assessments (e.g. prolongation of survival). When a "variable" is captured or measured, there is no necessary sense that any evaluation or judgment is involved. However, when a variable is to be measured that obviously or actively pertains to subject status, which is always the concern of the physician, that variable becomes or will always be an assessment. The term assessment is intended to invoke some degree of evaluation or judgment concerning subject status. See also primary variable, secondary variable, supporting variable.

variance. A measure of the variability in a sample or population. It is calculated as the mean squared deviation (MSD) of the individual values from their common mean. In calculating the MSD, the divisor n is commonly used for a population variance and the divisor $n-1$ for a sample variance.

visit. A clinical encounter for a subject in a trial. Visits are frequently referred to as occurring on Day X or during Week Y; there may be gaps between visits, which can take place within an epoch or span an epoch.

vulnerable subjects. Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent. [ICH]

Warning Letter. A written communication from FDA notifying an individual or firm that the agency considers one or more products, practices, processes, or other activities to be in violation of the Federal FD&C Act, or other acts, and that failure of

the responsible party to take appropriate and prompt action to correct and prevent any future repeat of the violation may result in administrative and/or regulatory enforcement action without further notice. [FDA]

washout period. A period in a clinical study during which subjects receive no treatment for the indication under study and the effects of a previous treatment are eliminated (or assumed to be eliminated).

web browser. A computer program that interprets HTML and other Internet languages and protocols and displays Web pages on your computer monitor.

web page. A single page on a Web site, such as a home page.

web server. A computer program that delivers HTML pages or files. Sometimes the computer on which a server program runs is also referred to as a server.

web site. A collection of Web pages and other files. A site can consist of a single Web page, thousands of pages, or custom-created pages that draw on a database associated with the site.

weighting. An adjustment in a value based on scientific observations within the data.

well-being (of the trial subjects). The physical and mental integrity of the subjects participating in a clinical trial. [ICH]

withdrawal. The act of reducing the degree of participation by a subject in a clinical trial. Subjects may withdraw permission for Sponsor use of data derived from study participation, privacy waivers, informed consent, or withdraw from active treatment component of a clinical trial but continue to be observed. Full withdrawal from participation in a study is called discontinuation.

within-subject differences. In a crossover trial, variability in each subject is used to assess treatment differences.

World Wide Web. All the resources and users on the Internet that are using HTTP protocols. Also called the Web and www.