

Glossary

Clinical Trials Terminology

The following glossary of clinical trial terms is the third produced by the Glossary Group of CDISC. Version 3.0 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* (ACT). As did the second version, this third 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 acronyms, abbreviations, and initials has also been compiled by CDISC, and follows this terminology glossary.

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)]
- NOTE: notes add usage conventions and relevant domain information to the definitions
- (“see also” statements)
- (Synonyms)

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

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

administrative record. A document/attributed collection of data detailing or recording an aspect of a study or its associated protocol that is not required by a regulatory agency. [PSM]

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 *inclusion criteria*.

adverse drug experience. See *adverse drug reaction*.

adverse drug reaction (ADR). In the pre-approval 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] NOTE: For further information, see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. See *unexpected adverse drug reaction*. Synonyms: *adverse reaction, adverse drug reaction, adverse drug experience*.

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.
[COMP/ICH/135/95] NOTE: For further information, see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.
Synonyms: side effect, adverse experience. See 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; 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. The likelihood that a relationship observed between 2 variables is due to chance. The probability of a Type 1 error. *See Type 1 error.*

amendment. A written description of a change(s) to or formal clarification of a protocol. [PSM, CDISC] *See Protocol Amendment.*

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]

analysis results. The output of the statistical analysis of the study data including tables, listings and figures. [PSM]

analysis set. The set of subjects whose data are to be included in the main analyses. This should be defined in the statistical section of the protocol. [ICH E9]

analysis variables. Variables used to test the statistical hypotheses identified in the

protocol and analysis plan; variables to be analyzed. [PR Group] *See variable.*

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. [CDISC] *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 defining the course of participation for a subject in a trial. [FDA, CDISC, SDS] *AG PSM definition: A unique sequence of trial design elements, including specification of the details of the planned observation or intervention. Each treatment group is assigned to one arm of the study.*

arm. Planned sequence of elements typically equivalent to a treatment group. [SDTM] *See element.*

assessment. A measurement, evaluation or judgement for a study variable pertaining to the status of a subject. NOTE: 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. *See variable, outcome, endpoint.*

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 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]

background material. Materials that serve to inform about information pertinent to the trial as described in the protocol. [PSM modified] NOTE: Examples include: literature reviews, history, rationale.

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.

baseline characteristics. The data representing values and observations of

subjects prior to exposure to protocol-required interventions. Used as comparators to determine efficacy and safety of investigational product. NOTE: Randomized, controlled trials aim to compare groups of participants that differ only with respect to the intervention (treatment). Although proper random assignment prevents selection bias, it does not guarantee that the groups are equivalent at baseline. Any differences in baseline characteristics are, however, the result of chance rather than bias. The study groups should be compared at baseline for important demographic and clinical characteristics. Baseline data may be especially valuable when the outcome measure can be measured at the start of the trial. [CONSORT Glossary]

baseline imbalance. Systematic error in creating intervention groups, such that they differ with respect to prognosis. That is, the groups differ in measured or unmeasured baseline characteristics because of the way participants were selected or assigned. Also used to mean that the participants are not representative of the population of all possible participants. [ICH E9]

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 *Type 2 error*.

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

bias. Systematic distortion of the estimated intervention effect away from the “truth,”

caused by inadequacies in the design, conduct, or analysis of a trial. [ICH E9, Consort Glossary]

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 drugs with the same active ingredient(s) 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. [AC T]

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 *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. Prevent identification of treatments/procedures/test to test subjects or study personnel results in order to limit bias (e.g., open-label, single-blind, double-blind). [ICH E9, EUDRACT]

brand name. Proprietary name for use in marketing a drug/device product, as approved by naming authority. [CDISC]

browser. Computer program that runs on the user's desktop computer and is used to navigate the World Wide Web. See *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 *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 *database lock*, *clean file*.

clean file. When all data cleaning is completed and database is ready for quality review and unblinding.

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 *self-evident change*.

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

clinical document. Documentation of clinical observations and services. An electronic document should incorporate the following characteristics: Persistence, Stewardship, Potential for authentication, Wholeness, and Human readability. [HL7]

clinical document architecture (CDA).

Specification for the structure and semantics of “clinical documents” for the purpose of exchange. [2001/20/EC, GCP, ANSI/HL7 CDA R1.0-2000]

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. Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one of more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s), and/or to study absorption, distribution, metabolism and excretion of one of more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. [2001/20/EC, GCP]

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/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.*

Clinician Reported Outcome (CRO). Clinician assessment of patient outcomes. It is based on objective and/or subjective data evaluated by the clinician. [DIA ePRO working group]

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

Combination Product. 1) A product containing two or more individual products; 2) Two or more separate products packaged together in a single package or as a unit. 3) A product that is packaged separately but is used only with another product.

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 investigational 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*.

confidence interval. A measure of the precision of an estimated value. The interval represents the range of values, consistent

with the data, that is believed to encompass the “true” value with high probability (usually 95%). The confidence interval is expressed in the same units as the estimate. Wider intervals indicate lower precision; narrow intervals, greater precision. [CONSORT Glossary]

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 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.

covariate. Factor or condition that influences outcome of a trial.

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 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 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 independent data-monitoring committee.*

data clarification. Answer supplied by the investigator in response to a query. Note: The investigator may supply a new data point value to replace the initial value or a confirmation of the queried data point. [CDISC]

data clarification form. A form used to query investigator and collect feedback to resolve questions re: data. [CDISC]

data collection instrument. Substrate upon, or through, which data are transcribed, recorded, processed at the point of patient care.

data element. Data contained within a narrative of a document section and provided in a mark up mode to allow machine processing. The mark-up or tagging facilitates document indexing, search and retrieval, and provides standard conventions for insertion of codes. [FDA-GL/IEEE]

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. An attribute of data pertaining to clinical trials depending on the quality of processes for data capture, correction, maintenance, transmission, and retention. Key dimensions of data integrity include that data be attributable, legible, contemporaneous, original and accurate. [FDAGL/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 *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 manager. Person or organization responsible for the collection, review and editing of study data. [PSM]

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

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

data quality. Given the absence of generally accepted specifications, data quality is generally defined based upon “fitness for use”—the degree to which data meet needs or expectations rather than conformance to a set of specifications. In the context of a clinical study, this is associated with an investigator or reviewer. Databases must be able to support meaningful conclusions and interpretations and demonstrate the relationship between the study protocol and the procedures actually followed and support analyses used to evaluate the study hypotheses. Quality is validated through internal and external benchmarking, quality control and auditing. See *ALCOA*. *Synonym: Compare to Data Integrity.*

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

data selection criteria. The rule by which a particular piece of data is selected and/or transferred between the point of care and the patient record; subsequently, from the patient record to the database; from database to inclusion in sub-population analyses. [Modified PSM]

data transformations. clinical trial conducted according to a single protocol but at more than one site, and, therefore, carried out by more than one investigator. [E9]

data type. Data types define the structural format of the data carried in the attribute and influence the set of allowable values an attribute may assume. [HL7]

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. A collection of data or information, typically organized for ease and speed of search and retrieval.

database lock. When all clinical trial data have been reviewed, queries resolved and issues addressed. At this point, the database can't be modified and data are considered to be ready for analysis. [CDISC] *Synonym: database freeze.*

decision rule. Succinct statement of how a decision will be reached based upon; the expected/foreseen clinical benefits in terms of outcomes of the primary endpoint. [FDA documentation]

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 variable. New variables created as functions of existing variables and/or application of mathematical functions. See *variable*.

design configuration. Clinical trial design developed to most appropriately compare treatment groups in a clinical trial. The configuration is based on randomization to one or more treatment arms, each arm being allocated a different (or no) treatment. [ICH, E9]

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 *drug development process*.

development plan. An ordered program of clinical trials, each with specific objectives (see ICH E8). Should be specified in a clinical plan, or a series of plans, with appropriate decision points and flexibility to allow modification as knowledge accumulates [Adapted from ICH E9]
Synonym: A document that describes the collection of clinical studies that are to be performed in sequence, or in parallel, with a particular active substance, device, procedure, or treatment strategy, typically with the intention of submitting them as part of an application for a marketing authorization.

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, prior to completion of all protocol-required elements, in a trial by an enrolled subject. [CDISC]

discrepancy. The failure of a data point 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 *ADME*.

document, type, class, element, etc. An ordered presentation of data, possibly including text and tabular analyses,

description, and ordered presentation. [PSM (modified); CDISC]

document root. The element in an XML document that contains all other elements; the first element in the document. [HL7 (SPL)]

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. 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]

dosage form. Physical characteristics of drug, (ex: tablet, capsule, or solution) that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients. [21 CFR §314.3]
Synonym: drug product

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 strength. Proportion of active substance to excipient, measured in units of volume or concentration. The strength of a drug product tells how much of the active ingredient is present in each dosage. [second definition: FDA Glossary of Terms]

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 Markup Language (HTML) that are more responsive to user interaction than previous versions of HTML.

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. [CDISC] *Synonyms: eClinical study; eClinical investigation.*

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.

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. An auditable process, usually automated, of assessing the content of a data field against its expected logical, format, range or other properties that is intended to reduce error.

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 (and patient population) for which it is designed. [AC T]

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 *data entry*, *data acquisition*.

electronic record. Any combination of text, graphics, data, audio, pictorial, or any other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system. [FDA Computerized Systems used in Clinical Trials, 21 CFR Part 11.3 (7)]

electronic signature. A computer data compilation of any symbol or series of symbols, executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual’s handwritten signature. [FDA Computerized Systems used in Clinical Trials, 21 CFR Part 11.3 (7)]

electronic source (eSource) data and document. Source Data or document initially captured electronically without an original paper record. [DIA ePRO Working Group]

element. 1) Basic building block for time within a clinical trial and comprises the following characteristics: A description of what happens to the subject during the Element. A definition of the start of the Element. A rule for ending the Element. 2) A section of text in an XML document delimited by start and end tags; or, in the case of empty elements (elements with no content, only attributes) indicated by an empty tag. [1) PSM, 2) HL7]

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. Variable that pertains to the efficacy or safety evaluations of a trial. [AC T] 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 *variable*.

enroll. transitive and intransitive. NOTE: Informed consent precedes enrollment, which precedes or is contemporaneous with randomization.

enrollment (cumulative). “Cumulative enrollment” means both current enrollment as well as any ever enrolled subjects who have ended participation.

enrollment (current). “Current enrollment” means the subjects actively continuing to participate in the trial as of the current date.

enrollment (target). “Target enrollment” means the number of subjects in a class or group (including the total for the entire trial) intended to be enrolled in a trial. NOTE: 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.

entities (persons, organizations). A physical thing or group of physical things that exist. [PSM, CDISC]

epoch. An interval of time in the planned conduct of a study during which the treatment is consistent. [SDS] NOTE: There are no gaps between epochs in a trial; they are defined in terms of treatment. For example a “baseline epoch” may specify that subjects not take any medications; a “treatment” epoch may specify that subjects all be subject to the same treatment regimen such as study drug supplemented with rescue medications. *Synonyms: period, cycle, phase, stage.* See *arm, visit*.

ePRO. PRO data initially captured electronically. [DIA ePRO Working Group] NOTE: usually ePRO data is captured as electronic source data.

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]

error rate. The error count divided by the data field count. NOTE: Errors may be categorized into a number of different types (e.g. errors requiring resolution by the site, errors such as spelling that are obvious and can be corrected in-house, errors in primary efficacy data). *Synonyms: Differences in calculated error rates occur not so much because of differences in the definition but because of inaccuracies in quantitating of the number of errors and differences in how the field count is calculated and benchmarked (e.g., how one deals with duplicate data or non-responded fields)*

eSource custodian. Sometimes referred to as a Trusted Third Party. This entity is an impartial organization, working on the behalf of the investigator and/or sponsor. It supplies a technical and reliable means of carrying out, facilitating, and producing, independent evidence about electronic data and records. [DIA ePRO Working Group] NOTE: There is no current legal basis for an eSource Custodian.

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

established name. The official name of a drug substance. [FD&C, ACT]

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

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

e valuable (for efficacy and safety). Whether data or subjects meet Statistical Analysis Plan criteria for inclusion in Efficacy/Safety datasets.

event. A subject visit or other encounter where subject data are collected, generated or reviewed. [PSM] See *subject data event*.

exclusion criteria. List of [characteristics] in a protocol, any one of which [may] exclude a potential subject from participation in a study.

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

explanatory trial. Term used to describe a clinical study designed to demonstrate the efficacy of a product. See *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 *TCP/IP*.

final 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 analyses are fully integrated into a single report. [ICH E3]

finding. Conclusion based on data collected during clinical trial. Noteworthy or remarkable data element.

first subject/patient in (FSI/FPI). Date and time that the first subject is enrolled in a clinical trial. See *enroll*.

first subject treated. Date and time that the first subject receives the test article or

placebo in a clinical trial. [Derived from CDISC/ACT definition of FDSI/FPI]

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 I 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 *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 re: Male/Female. [IOM]

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]

generic name. The drug identifying name to which all branded (proprietary) names for that indication are associated. [CDISC]

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 COMP/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*.

granularity. The relative size of a defined unit; in the context of this specification, granularity refers to the size of an information unit where it would be coarse grained and a data point would be fine grained.

group sequential design. A design which includes one or more interim analyses while maintaining the overall Type 1 error among all analyses.

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). An ANSI-accredited Standards Developing Organization (SDO) operating in the healthcare arena. [HL7] NOTE: Level 7 refers to the highest level of the International Standards Organization's (ISO) communications model for Open Systems Interconnection (OSI) the application level. The application level addresses definition of the data to be exchanged, the timing of the interchange, and the communication of certain errors to the application. Level 7 supports such functions as security checks, participant identification, availability checks, exchange mechanism negotiations and, most importantly, data exchange structuring [HL7]

healthcare provider. One who directly or indirectly administers interventions which are designed to improve the physical or emotional status of patients. [CDISC]

healthy volunteer. Subject (not a patient) in a clinical trial. NOTE: Usually healthy volunteers serve as subjects in Phase I trials. [ACT2]

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

HyperText Markup Language (HTML). A specification of the W3C that provides markup of documents for display in a Web browser. [HL7]

hypothesis to test. In a trial, a statement relating to the possible different effect of the interventions on an outcome. The null hypothesis of no such effect is amenable to explicit statistical evaluation by a hypothesis test, which generates a P value. [CONSORT glossary]

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 *exclusion criteria*.

independent data monitoring committee (IDMC). A committee established by the sponsor to assess at intervals the progress of a clinical trial, safety data, and critical efficacy variables and recommend to the sponsor whether to continue, modify, or terminate the trial. [ICH 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 *institutional review board*.

indication. The specific primary reason for which the investigational product is being administered.

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 *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 the basis of the intention to treat a subject (i.e., the planned treatment regimen) rather than the actual treatment given. [ICH E9]

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(es). Analysis comparing intervention groups at any time before the formal completion of the trial, usually before recruitment is complete. [CONSORT glossary]

interim analysis schedule. The time/information points at which interim analyses are planned.

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

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).

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] NOTE: CDISC includes test articles in its definition of investigational products.

investigational treatment. 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] NOTE: 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 *sponsor-investigator*.

investigator/institution. An expression meaning "the investigator and/or institution, where required by the applicable regulatory requirements." [ICH E6 1.35]

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 item, such as a single systolic blood pressure. [ACT] NOTE: Items are collected together as an item group.

item definition. The definition of a question and the specification of the format and semantics of the response. [ODM]

label. Description of a drug product/device that includes: the indication, who should use it, adverse events, instructions for use,

and safety information. [FDA] NOTE: Labels must be approved by regulatory authorities. *Synonyms: package insert, patient package leaflet.*

labeling (content of). All text, tables and figures in labeling as described in regulations for a specific product (e.g., 21CFR 201.56 and 201.57 for human prescription drugs, 201.66 for human over-the-counter drugs).

laboratory (clinical). A laboratory providing analyses of samples collected in clinical care or research. [CDISC]

last subject out/complete (LSC/LPC or LSO/LPO). Date and time that the last patient completes a trial (all data collected). *See subject, patient, completion.*

last subject/patient in (LSI/LPI). Date and time that the last subject to participate in a clinical trial is enrolled. *See enroll.*

legal authentication. A completion status in which a document has been signed manually or electronically by the individual who is legally responsible for that document. [HL7]

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.

Level. A quantum set of specializations within the CDA. [HL7]

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. Clinical studies that are designed to improve the sales of a product or to show potential buyers the rationale for purchase. [CDISC, ACT2

Modified]. NOTE: Many market support trial outcomes are used for additional indications of already approved drugs, publications and promotion purposes. *See outcomes.*

markup. Computer-processable annotations within a multimedia document. [HL7] NOTE: In the context of the HL7 specification, markup syntax is according to the XML Specification.

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 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.

Message(HL7). The atomic unit of data transferred between systems. It is comprised of a group of segments in a defined sequence. Each message has a

message type that defines its purpose. [PSM CDISC, HL7] NOTE: For example, the Admission, Discharge and Transfer (ADT) Message type is used to transmit portions of a patient's ADT data from one system to another. In HL7, a three character code contained within each message identifies its type.

meta-analysis. A statistical process for pooling data from multiple clinical trial and summarizing results through formal statistical means.

metabolism. The sum of the processes by which a substance is handled in the living body. *See ADME.*

metadata. Data that describes other data.

migration. The act of moving a system or software product (including data) from an old to new operational environment in accordance with a software quality system. [ISO/IEC/IEEE 12207:1995 §5.5.5]

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 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. Clinical trial conducted according to a single protocol but at more than one site, and, therefore, carried out by more than one investigator. [ICH E9 Glossary] *Synonym: multicenter study.* See *investigator/institution*.

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-approve 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 *research hypothesis*.

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

objective. The reason for performing a trial in terms of the scientific questions to be answered by the data collected during the trial. [CDISC] NOTE: The primary objective is the main question to be answered and drives any statistical planning for the trial (e.g., calculation of the sample size to provide the appropriate power for statistical testing). Secondary objectives are goals of a trial that will provide further information on the use of the treatment.

objective measurement. A measurement of a physiological or medical variable such as blood glucose levels that is obtained by a measuring device rather than human judgement or assessment. [CDISC] See *outcome*, *patient reported outcome*; *objective measures are observations (SDTM)*, and *could be endpoints*. *Patient reported outcomes are subjective measurements*.

observation. 1) An assessment of patient condition or analysis of data collected on an individual patient or group of patients. 2) (SDTM) A discrete piece of information collected during a study. [Consolidated Glossary; SDTM] NOTE: Observations (meaning 1) are required by protocol (e.g., require evaluation of patient or data by investigator/staff). Such planned observations are typically distinguished from anecdotal comments noted during a clinical trial (which qualify as observations under meaning 2). See *variable*; *referring to an ad hoc comment as an observation is colloquial*.

observer assessment. An assessment of patient condition made by an observer (investigator, nurse, clinician, family member, etc.). [ePRO Workgroup] NOTE: Distinguished from self-assessment. The observer relies on his or her judgment to assess the subject. An interviewer simply

capturing subject self assessments is not an observer. *Compare to PRO*.

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 *open study*.

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

origin. 1) Source of information collected in the course of a clinical trial. Specifically used to differentiate between data collected at point of patient contact and data that are derived or calculated. 2) (SDTM) A metadata attribute defined for each dataset variable in the "Define" document of an SDTM submission that refers to the source of a variable. (e.g. CRF, derived, sponsor defined, PRO, etc.). [Consolidated Glossary, SDTM for descriptions of the Define document] NOTE: See SDTM "Model concepts and terms."

original medical record. See *source documents*.

outcome. Events or experiences that clinicians or investigators examining the impact of an intervention or exposure measure because they believe such events or experiences may be influenced by the intervention or exposure. [Dept. Epidemiology & Statistics, McMaster University; SDTM] NOTE: Such events and experiences are called clinical outcomes independently of whether they are part of the original question/protocol of the investigation. See *variable*; *can be result of analysis*; *is more general than endpoint in that it does not necessarily relate to a planned objective of the study*.

outcome (of event). Refers to the resolution of an adverse event. [SDTM Events class of observation] NOTE: often denoted using a pick list from a controlled terminology such as Recovered/resolved, recovering/resolving, not recovered/not resolved, recovered/resolved with sequelae, fatal, or unknown.

outcomes research. Research concerned with benefits, financial costs, healthcare system usage, risks, and quality of life as

well as their relation to therapeutic interventions. [Guyatt GH, Feeney DH, Patrick DL. Measuring health-related quality of life. *Ann Internal Medicine* 1993; 118:622-629] NOTE: usually distinguished from research conducted solely to determine efficacy and safety. See *pharmacoeconomics*, *quality of life*.

outliers. Data anomalies which are extreme from a univariate or multivariate perspective.

overview. See *meta-analysis*. [ACT2]

p-value. Study findings can also be assessed in terms of their statistical significance. The *P* value represents the probability that the observed data (or a more extreme result) could have arisen by chance when the interventions did not differ. [CONSORT Glossary ACT2 modified]

packaging. The material, both physical and informational, that surrounds an active therapeutic agent once it is fully prepared for release to pharmacies and to patients. [CDISC]

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 *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 variable in a model, or a variable that wholly or partially characterizes a probability distribution (mathematics and statistics). [CDISC PR group, Parexel Barnett] NOTE: In clinical trials the term is often used synonymously with “variable” for factual information (age, date of recovery), measurements, and clinical assessments. It is most appropriately linked to statistical conventions and as a numeric characteristic of a population. Thus the term is narrower than variable. See *variable*, *outcome*.

participant. A person or entity with a role in healthcare or a clinical study. [PSM CDISC] NOTE: Participants in a clinical trial may

include subjects, study personnel, patients, and others. A subject participates as part of the group of people who are administered the therapeutic intervention or control. Patients in a clinical trial are subjects who are also under medical care for the indication under study. See Role in the context of HL7 RIM. See *subject*, *patient*.

patient. Person under a physician's care for a particular disease or condition. [ACT2] NOTE: A subject in a clinical trial is not necessarily a patient, but a patient in a clinical trial is a subject. See *subject*, *trial subject*, *healthy volunteer*. Often used interchangeably as a synonym for subject but healthy volunteers are not patients.

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.

patient reported outcome (PRO). Report coming directly from patients or subjects through interviews or self-completed questionnaires or other data capture tools such as diaries about their life, health condition(s) and treatment. [CDISC, DIA ePRO Workgroup, reviewed with Gordon Guyatt and Holger Schuneman; Donald L. Patrick (Patient-Reported Outcomes (PROs): An Organizing Tool for Concepts, Measures, and Applications. MAPI Quality of Life News Letter 31: 1-5, 2003) (Acquardo C., Berzon C., et. al. Incorporating the Patient's Perspective into Drug Development and Communication: An Ad Hoc Task Force Report of the Patient-Reported Outcomes (PRO) Harmonization Group Meeting at the Food and Drug Administration, Feb. 16, 2001. *Value in Health* 6 (5): 522-531, 2001.)] NOTE: PROs are used to assess outcomes involving the patients'/subjects' perceptions, symptoms, satisfaction with treatment, adherence to prescribed regimens. Historically observations on patients have been made by observers, which has produced scientific records lacking high quality data on subjective symptom intensity, perceived benefit, etc. PROs include outcomes recorded by interviewers transcribing the views expressed by the patient, but the term does not apply to outcomes recorded by observers who rely on their own judgment. *Synonyms:* *subject reported outcomes*. See *outcome*, *subject*, *patient*.

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

permanent data. A “state” of data that is permanent and becomes part of an electronic record. “Permanent” implies that any changes made to the electronic data are recorded via an audit trail and not obscured. [DIA ePRO Working Group].

per protocol analysis set. The set of data generated by the subset of subjects who complied with the protocol sufficiently to ensure that these data would be likely to exhibit the effects of treatment according to the underlying scientific model. [ICH E9]

pharmacodynamics. 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.

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

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

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. *Compare to pharmacogenetic test*.

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. 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.

phase. 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. [ACT2]

Phase I. The initial introduction of an investigational new drug into humans. Phase I studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. [FDA] NOTE: 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 I, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase II studies. The total number of subjects and patients included in Phase I studies varies with the drug, but is generally in the range of 20 to 80. Phase I 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.

Phase II. 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. [FDA] NOTE: Phase II studies are typically well controlled, closely monitored, and conducted in a relatively small number of

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)

patients, usually involving no more than several hundred subjects.

Phase III. 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. [FDA] NOTE: Phase III studies usually include from several hundred to several thousand subjects.

Phase IIIb. Phase IIIb studies are a sub category of Phase III trials near the time of approval to elicit additional findings. [FDA]

Phase IV. Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain postmarketing (Phase IV) studies to delineate additional information about the drug's risks, benefits, and optimal use. [FDA] NOTE: These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase II

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.

Phase V studies. Postmarketing surveillance is sometimes referred to as Phase V. [ACT2] See *outcomes research*.

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 IV studies*, *Phase V studies*.

pragmatic trial. Term used to describe a clinical study designed to examine the benefits of a product under real world conditions. [ACT2]

protocol approval. Marks completion of protocol development and occurs when the signature of the last reviewer on the protocol approval form has been obtained, signifies that all reviewer changes to the protocol have been incorporated. [ACT2, CDISC] NOTE: Approval by the sponsor

psychometric reliability. The consistency of the scores of a measure. Reliability does not imply validity or accuracy. For example, test-retest reliability measures the ability of a measure to produce the same score when a test is re-administered to patients who have not changed with respect to the measurement

quality of life. A broad ranging concept that incorporates an individual's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationships to salient features of the environment. [The WHO Group. The Development of the World Health Organization Quality of Life assessment instrument (WHOQOL). In Orley J & Kuyken

W. (Eds.) Quality of Life Assessment: International Perspectives. Springer-Verlag: Berlin, Heidelberg 1994: 41.] NOTE: The growing sense of wanting to measure the benefits and negative impact of an “improvement” in a physiologically measured symptom is addressed by this branch of research seeking to quantify what an intervention means in the daily life and feelings of a patient.

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 E6 1.48] NOTE: Unequal randomization is 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 *balanced study*.

raw. Data as originally collected. Distinct from

Derived. [CDISC Study Data Tabulation Model, Version 1.0]

raw data. Records of original observations, measurements, and activities (such as laboratory notes, evaluations, data recorded by automated instruments) without conclusions or interpretations. [ACT] Researcher’s records of subjects/patients, such as patient 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] [CDISC version 1]] See *eSource*.

RCRIM. Regulated Clinical Research and Information Management, which is a Technical Committee within HL7 (an acronym pronounced “arcrim”).

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.

Reference Information Model (RIM). An information model used as the ultimate defining reference for all HL7 standards. [HL7]

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.*

reliability, psychometric. See *psychometric reliability*.

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 *null hypothesis*.

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

retrospective. Capture of clinical trial data is retrospective when it is recalled from memory rather than captured contemporaneously in real-time. [Modified ACT2, CDISC GG] NOTE: Retrospective capture is important in PRO’s because of “recall bias” and other errors documented in psychological research comparing contemporaneous self reported assessments and those that rely on recall from 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.

role. 1) The function or responsibility assumed by a person in the context of a clinical study. Examples include Data Manager, Investigator. 2) classifier for variables that describe “observations” in the SDTM. Role is a metadata attribute that determines the type of information conveyed by an observation-describing variable and standardizes rules for using the describing variable. [1] CDISC harmonization with the HL7 RIM, PSM 2) SDTM concepts and terms] See *functional role*.

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 failure. Potential subjects who did not meet one or more criteria required for participation in a trial. [CDISC] See *screening of subjects*.

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

screening of subjects. A process of active consideration of potential subjects for enrollment in a trial. "Screening failures" are potential subjects who did not meet one or more criteria required for participation.

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 trials. Trials conducted to detect persons with early, mild and asymptomatic disease. [CDISC GG]

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 objective. See *objective*. [CDISC]

secondary variable. The primary outcome is the outcome of greatest importance. Data on secondary outcomes are used to evaluate additional effects of the intervention. [CONSORT Glossary] *Synonyms:* *outcome, endpoint*.

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.

semantic. In the context of a technical specification, semantic refers to the meaning of an element as distinct from its syntax. Syntax can change without affecting semantics. [HL7]

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 *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 *serious adverse event*.

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

sex. Maleness or Femaleness, as defined by chromosomal makeup. See *gender*.

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 *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 *blind study, double-blind study, triple-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.

software validation. Confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through software can be consistently fulfilled. [General Principles of Software Validation; Final Guidance for Industry and FDA Staff, Jan 11, 2002. ISO/IEC/IEEE 12207:1995 §3.35; 21 CFR 820.20; 21CFR11.10(a); ISO 9000-3; Huber, L. (1999) In Search of Standard Definitions for Validation, Qualification, Verification and Calibration. BioPharm 12:(4)56-58.] NOTE: Validating software thus should include evaluation of the suitability of the specifications to "ensure user needs and intended uses can be fulfilled on a consistent basis" (21 CFR 820.20). See *validation, verification*. *Verification also concerns confirmation that specified requirements have been met, but typically is used for tracing requirements and evidence of conformance in the individual phases or modules rather than suitability of the complete product.*

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 document verification. The process by which the information reported by an investigator is compared with the original records to ensure that it is complete, accurate and valid. [Schuyt and Engel, DIA Journal 33: 789-797, 1999; Khosla et al. Indian J. Pharm 32:180-186, 2000]

Synonym: SDV. See validation of data.

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]

special populations. Subsets of study populations of particular interest included in clinical trials to ensure that their specific characteristics are considered in interpretation of data [e.g., geriatric]. [FDA ; CDISC PR]
Synonym: SDV. See validation of data.

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. A guideline for medical management and treatment. [CDISC GG]

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 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.

stratification. Grouping defined by important prognostic factors measured at baseline. [ICH E9]

study. See *clinical trial*. NOTE: Occasionally refers to a project of several related clinical trials. [CDISC GG]

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 coordinator. See *clinical research coordinator*.

study description. Representation of key elements of study; eg, control, blinding, gender, dose, indication, configuration.

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; 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. [[CDISC] [Modified from Pocock, Clinical Trials: A Practical Approach] See *trial design model*, *arm*, *epoch*, and *visit*.

study design rationale. Reason for choosing the particular study design.

study design schematic. Diagrammatic representation of key activities within the study.

study design schematic. Diagrammatic representation of key activities within the study.

study population. Defined by protocol inclusion/exclusion criteria.

study protocol. See *protocol*.

study variable. A term used in trial design to denote a variable to be captured on the CRF. See *variable*.

sub-investigator. Any 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 *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-reported outcome (SRO). An outcome reported directly by a subject in a clinical trial. [Donald L. Patrick (Patient-Reported Outcomes (PROs): An Organizing Tool for Concepts, Measures, and Applications. MAPI Quality of Life News Letter 31:1-5, 2003] See *patient-reported outcome (PRO)*.

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 *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]

supplier. An organization that enters into a contract with the acquirer for the supply of a system, software product, or software service under the terms of a contract. [ISO/IEC/IEEE 12207:1995 §3.30]

surrogate marker. A measurement of a drug's biological activity that substitutes for a clinical endpoint such as death or pain relief. [ACT2]

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]

syntactic. Order, format, content of clinical trial data and/or documents as distinct from the meaning. NOTE: syntactic interoperability is achieved when information is correctly exchanged between two systems according to structured rules whether or not sensible meaning is preserved. [CDISC GG] *Synonyms:* cf *semantic*, *semantic interoperability*.

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. A 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. [CDISC GG] *Synonym:* *vendor*.

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

terminology. A standardized, finite set of terms (e.g. picklists, ICD9 codes) that denote patient findings, circumstances, events, and interventions. NOTE: The terms should have sufficient detail to support clinical research, healthcare decisions, outcomes research and quality improvement. Standardization should be sufficient that the same set of terms may be extended to administrative, regulatory, and fiscal applications. [JJ Camino] *Compare to Glossary, which is a list of words and their definitions pertaining to usage in a particular field or context.*

transcription. Process of transforming dictated or otherwise documented information from one storage medium to another [HL7, ACT2] NOTE: often data is transcribed from source docs to CRFs or to eCRFs.

transient data. A “state” of data being used internally by the system without ever being permanently stored. [Paraphrased from PDA/ISPE—Good Practice and Compliance for Electronic Records and Signatures Part 2 § Appendix 9, transient data And §4.5, transient data] See *permanent data*.

transient data collector. Processes and devices that acquire transient data. [DIA ePRO Working Group]

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 design model. Defines a standard structure for representing the planned sequence of events and the treatment plan of a trial. NOTE: a component of the SDTM that builds upon elements, a ms epochs, visits; suitable also for syntactic interpretation by machines. [CDISC GG] See *study design*.

trial monitoring. Oversight of quality of

study conduct and statistical interim analysis. [ICH E9]

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]

trial subject. Subject in a clinical trial. [ACT] See *participant*, *patient*, *subject*.

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.

type of comparison. eg, Safety, Efficacy, PK/PD. [ICH E9, EUDRACT (p,18)]

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. See *randomization*.

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 *adverse drug reaction*.

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

valid. 1) Sound. 2) Well grounded on principles of evidence. 3) Able to withstand criticism or objection. [FDA Glossary of Computerized System and Software Development Terminology]

validation. 1) Process of establishing suitability to purpose. 2) For software and systems, establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes. [CDISC, FDA Glossary of Computerized System and Software Development Terminology]

validation of data. 1) A 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. 2) The checking of data for correctness or compliance with applicable standards, rules, and conventions. NOTE: meaning 1) is not “data verification” but meaning 2) could be. [1] ISO; 2) FDA Glossary of Computerized System and Software Development Terminology] See *source document verification*.

validity. See *validation*.

validity, psychometric. See *psychometric validation*.

variable. 1) Any quantity that varies; any attribute, phenomenon or event that can have different qualitative or quantitative values. 2) in SDTM “variables” are used to describe observations. Such describing variables have roles that determine the type of information conveyed by the variable about each observation and how it can be used. NOTE: 1) There is usually a form of metadata that goes with the variable, there is a variable definition that describes what is varying, and there is a value for the variable. In the context of a protocol, variables pertain to the study. 2) in SDTM a “study variable” would be an observation. [CDISC GG]

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 that encompasses planned and unplanned trial interventions, procedures and assessments that may be performed on a subject. A visit has a start and an end, each described with a rule. NOTE: For many domains each visit results in one record per visit. [SDTM, Trial Design Model]

verification. 1) The act of reviewing, inspecting, testing, checking, auditing, or otherwise establishing and documenting whether items, processes, services, or documents conform to specified requirements. 2) (of software) provides objective evidence that the design outputs of a particular phase of the software development life cycle meet all of the specified requirements for that phase. [General Principles of Software Validation; Final Guidance for Industry and FDA Staff, Jan. 11, 2002. ANSI/ASQC A3-1978; ISO/IEC Guide 25]

verification of data. See *source document verification*.

volunteer. A person volunteering to participate as a subject in a clinical trial, often a healthy person agreeing to participate in a Phase I trial. [CDISC GG] See *Phase I*.

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.