

CDISC Clinical Research Glossary

Version 7.0

Glossary Terms

510(k). Premarket Notification (PMN) required for certain medical devices. See <http://www.fda.gov/cdrh/510k/home.html>

abbreviation. A set of letters that are drawn from a word or from a sequence of words and that are used for brevity in place of the full word or phrase. NOTE: An abbreviation is NOT pronounced as a word, but each letter is read in sequence (e.g., NIH). *Compare to acronym.*

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

acronym. 1. A word formed from the beginning letters (e.g., ANSI) or a combination of syllables and letters (e.g., MedDRA) of a name or phrase. 2. The short set of letters that identify a clinical study protocol. NOTE: An acronym is usually pronounced as a word, not by speaking each letter individually. *Compare to abbreviation.*

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

activation. Enabling an eClinical trial system to capture data; usually used for EDC systems.

admission criteria. Basis for selecting target population for a

CDISC Glossary Project

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Orientation: The following Glossary is the seventh produced by the Glossary Project of CDISC, which seeks to harmonize definitions (including acronyms, abbreviations, and initials) used in the various standards initiatives undertaken by CDISC in clinical research. The purpose of the CDISC Glossary is also to serve the community of clinical researchers by selecting and defining terms pertaining to clinical research, particularly eClinical investigations, sponsored by the pharmaceutical industry or a federal agency. The Glossary is publicly accessible on the CDISC Web site (CDISC.org), where comments on the Glossary are welcomed.

Note that this CDISC Glossary is NOT comprehensive for all words bearing on human health, medicine, or laboratory methods. The Glossary includes references and links to other glossaries such as regulatory dictionaries and to health-related controlled terminologies that are known to be useful in conducting clinical research, including the CDISC Terminology Project.

Glossary terms are organized alphabetically by first word according to the opinion of the Glossary Project Team concerning most common usage in clinical research. Thus "source document verification" would appear under "source," not "verification." The

Glossary follows the practice of preceding certain terms with the letter "e" to denote that they pertain to electronic or Web implementation. Each term in the Glossary has the following conventions concerning content and order of presentation:

Term. The word or phrase being defined is followed by a period. Only proper nouns are capitalized.

Definition. Multiple meanings of the same term are numbered 1., 2., 3., etc.

NOTE: Comments including usage or domain knowledge related to a term may follow the definition.

Source(s). The sources for definitions are cited (see "Reference Citations") in square brackets. Where the definition has been altered by CDISC, the citation states "modified from." Where the definition has been drawn by CDISC from text that is not itself a definition, the citation states "after" or "from." Where no source is listed, the definition is from CDISC.

Related terms. Some definitions offer synonyms (See), comments, or related terms (See also or Compare to) to sharpen or expand upon the definition.

*See Reference Citations, p. 52, for Glossary Project Team Members

clinical trial. Subjects must be screened to ensure that their characteristics match a list of admission criteria and that none of their characteristics

match any single one of the exclusion criteria set up for the study. *See also inclusion criteria, exclusion criteria.*

adverse drug experience.

See *adverse drug reaction*.

adverse drug reaction (ADR). Any noxious and unintended response associated with the use of a drug in humans. 1. Post-approval: an adverse event that occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function. 2. Pre-approval: an adverse event that occurs at any dose and where a causal relationship is at least a reasonable possibility. NOTE: FDA 21 CFR 310.305 defines an adverse drug experience to include any adverse event, "whether or not considered to be drug-related." CDISC recognizes that current usage incorporates the concept of causality. [WHO Technical Report 498(1972); ICH E2A]

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. NOTE: For further information, see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. "[Modified from ICH E2A]" *Synonyms:* *side effect, adverse experience.* See also *serious adverse event, serious adverse experience.*

adverse experience. See *adverse event*.

adverse reaction. See *adverse drug reaction*.

algorithm. Step-by-step procedure for solving a mathematical problem; also used to describe step-by-step procedures for making a series of

choices among alternative decisions to reach a calculated result or decision.

alpha error. The likelihood that a relationship observed between 2 variables is due to chance. The probability of a Type 1 error. [Modified from AMA Manual of Style]

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

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 dataset. An organized collection of data or information with a common theme arranged in rows and columns and represented as a single file; comparable to a database table. NOTE: Standardizing analysis datasets is intended to make review and assessment of analysis more consistent [ADaM].

analysis set. A set of subjects whose data are to be included in the main analyses. This should be defined in the statistical section of the protocol. NOTE: There are a number of potential analysis sets, including, for example,

the set based upon the intent-to-treat principle. [ICH E9]

analysis variables. Variables used to test the statistical hypotheses identified in the protocol and analysis plan; variables to be analyzed. [PR Project] See also *variable*.

anchor. Designation for a planned activity, often marking the transition between epochs or elements of a clinical study plan (e.g., "FPFV—first patient first visit").

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

application software. See *application*.

application. 1. Computer application: software designed to fill specific needs of a user; for example, software for navigation, project management, or process control. 2. Regulatory application: application made to a health authority to investigate, market, or license a new product or indication. *Synonyms:* 1. *computer application, application software.*

approvable letter. An official communication from FDA to an NDA/BLA sponsor that lists issues to be resolved before an approval can be issued. [Modified from 21 CFR 314.3; Guidance to Industry and FDA Staff (10/08/2003)]

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 E6]

approval letter. An official communication from FDA to inform an applicant of a decision to allow commercial marketing consistent with conditions of approval. [Modified from 21 CFR 314.3; Guidance to Industry and FDA Staff (10/08/2003)]

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

assessment. A measurement, evaluation, or judgment 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*; the term assessment is intended to invoke some degree of evaluation or judgment concerning subject status.

audit. 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 E6 Glossary]

audit certificate. Document that certifies that an audit has taken place (at an investigative site, CRO, or clinical research department of a pharmaceutical company). [ICH E6 Glossary]

audit report. A written evaluation by the auditor of the results of the audit. [Modified from ICH E6 Glossary]

audit trail. A process that captures details such as additions, deletions, or alterations of information in an electronic record without obliterating the original record. An audit trail facilitates the reconstruction of the history of such actions relating to the electronic record. [after ICH E6, CSUIC]

back translation (natural language). The process of translating a document that was translated from one language to another back to the original language. Used to ensure that consent forms, surveys, and other clinical trial documents will be clear and accurate in the translated form.

background material. Information pertinent to the understanding of a protocol. NOTE: Examples include investigator brochure, literature review, history, rationale, or other documentation that places a study in context or presents critical features. [PR Project]

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 signal channels have a bandwidth.

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

baseline characteristics. Demographic, clinical, and other data collected for each participant at the beginning of the trial before the intervention is administered. 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 also be measured at the start of the trial. [CONSORT Statement]

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. NOTE: 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 Glossary]

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

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

bias. Situation or condition that causes a result to depart from the true value in a consistent direction. Bias refers to defects in study design or measurement. [AMA Manual of Style. See also *ICH E9, CONSORT Statement*]

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. NOTE: To be considered bioequivalent, the bioavailability of two products must not differ significantly when the two products are given in studies at the same dosage under similar conditions.

biological marker. See *biomarker*.

Biologics Licensing Application (BLA). An application to FDA for a license to market a new biologic product in the United States.

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. [Biomarker definitions working group]

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

blind review. Checking and assessing data prior to breaking the blind, for the purpose of finalizing the planned analysis. [Modified ICH E9]

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.

blinded study. A study in which the subject, the investigator, or anyone assessing the outcome is unaware of the treatment assignment(s). NOTE: Blinding is used to reduce the potential for bias. [Modified ICH E6 Glossary] See also *blinding/masking, double-blind study, single-blind study, triple-blind study; contrast with open-label or unblinded study*.

blinding. A procedure to limit bias by preventing subjects and/or study personnel from identifying which treatments or procedures are administered, or from learning the results of tests and measures undertaken as part of a clinical investigation. NOTE: Masking, while often used synonymously with blinding, usually denotes concealing the specific study intervention used. [from ICH E9] The term masking is often preferred to blinding in the field of ophthalmology. [from AMA Manual of Style]. See also *blinding, double-blind study, masking, single-blind study, triple-blind study. Contrast with open-label and/or unblinded study*.

branch. Point within a study design where there is an allocation of subject subsets to particular procedures or treatment groups.

brand name. See *proprietary name*. Synonyms: *trade name; proprietary name*. [SPL]

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

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

carry-over effect. Effects of treatment that persist after treatment

has been stopped, sometimes beyond the time of a medication's known biological activity.

case history. An adequate and accurate record prepared and maintained by an investigator that records all observations and other data pertinent to the investigation on each individual administered the investigational drug (device or other therapy) or employed as a control in the investigation. NOTE: 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 312.62b]

case record form. See *case report form*.

case report form (CRF). 1. 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. 2. A record of clinical study observations and other information that a study protocol designates must be completed for each subject. NOTE: 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 [ICH E6 Glossary]. See also *CRF (paper)*.

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

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

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

CDISC Standard (The). CDISC term for a proposed uniform CDISC standard intended to address the full life-cycle of a clinical trial including protocol representation, capture of source data, submission, and archiving using a set of fully integrated and consistent models, terms, and controlled vocabularies derived from the current set of CDISC standards.

certified copy. A copy of original information that has been verified as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original. NOTE: The copy may be verified by dated signature or by a validated electronic process. A *certified copy of a source document* may serve as a *source* for a *clinical investigation*. See also *source data*, *source*. [After CSUICI]

Certified IRB Professional (CIP). Certification awarded to persons who satisfy the educational and employment requirements and pass an examination conducted by the Applied Research Ethics National Association (ARENA), the membership division of Public Responsibility in Medicine and Research (PRIM&R).

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

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, usually running on a server, that fulfills the request. Web browsers (such as Netscape Navigator and Microsoft Explorer) are clients that request HTML files from Web servers.

clinical benefit. A therapeutic intervention may be said to confer clinical benefit if it prolongs life, improves function, and/or improves the way a subject feels.

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

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

clinical development plan. 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. NOTE: The plan should have appropriate decision points and allow modification as knowledge accumulates. [from ICH E9] See also *development plan*.

clinical document architecture. Specification for the structure and semantics of "clinical documents" for the purpose of exchange. [HL7; SPL]

clinical document. A documentation of clinical observations and services. NOTE: An electronic document should incorporate the following characteristics:

persistence, stewardship, potential for authentication, wholeness, and human readability. [SPL]

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

clinical investigation. See *clinical trial*, *clinical study*. NOTE: Increased usage of investigation or study in the U.S. rather than "trial," may reflect the appearance of the term in FDA regulations concerning clinical research activities.

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 a 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 on behalf of a site investigator, 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 intervention. NOTE: 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. The term "clinical significance" is not advisable unless operationally defined.

clinical study (trial) report. A written description of a 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. NOTE: For further information, see the ICH Guideline for Structure and Content of Clinical Study Reports. [ICH E6 Glossary]

clinical study. *See clinical trial.*

clinical trial. A research investigation involving human subjects that is designed to answer specific questions about the safety and efficacy of a biomedical intervention (drug, treatment, device) or new ways of using a known drug, treatment, or device. [modified from ICH E6 Glossary, Directive 2001/20/EC] *Synonym: clinical investigation or study.*

clinical trial data. Data collected in the course of a clinical trial. *See also 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). NOTE: 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.

clinician reported outcome. Clinician assessment of patient outcomes, based on objective or subjective data evaluated by the clinician.

codelist. Finite list of codes and their meanings that represent the only allowed values for a data item. *See also controlled vocabulary. A codelist is one type of controlled vocabulary.*

coding. In clinical trials, the process of assigning data to categories for analysis NOTE: Adverse events, for example, may be coded using MedDRA.

cognitive debriefing. A qualitative research tool used to determine whether concepts and items are understood by patients in the same way that PRO instrument developers intend. NOTE: Cognitive debriefing interviews involve incorporating follow-up questions in a field test interview to gain better understanding of how patients interpret questions asked of them and to collect and consider all concepts elicited by an item. [from PRO Draft Guidance Glossary]

cohort. 1. A group of individuals who share a common exposure, experience or characteristic. 2. A group of individuals followed-up or traced over time in a cohort study. [AMA Manual of Style]

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 Manual of Style] *See also prospective study.*

combination product. 1. A product comprising 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. [Modified from SPL Glossary]

common data element. A structured item characterized by a stem and response options together with a history of usage that can be standardized for research purposes across studies conducted by and for NIH. NOTE: The mark up or tagging facilitates document indexing, search and retrieval, and provides standard conventions for insertion of codes. [NCI, CaBIG]. *See also item.*

Common Technical Document. A format agreed upon by ICH to organize applications to regulatory authorities for registration of pharmaceuticals for human use. [ICH] *See also eCTD.*

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

comparator (product). An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical trial. [ICH E6 Glossary] *See also control.*

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.

completion. 1. Subject completion: the case where a subject ceases active

participation in a trial because the subject has, or is presumed to have, followed all appropriate conditions of a protocol. 2. Study completion: according to the study protocol, the point at which all protocol-required activities have been executed. [Modified EU CTD]

compliance (in relation to trials). Adherence to trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements. [Modified ICH E6 Glossary]

computer application. See *application*.

concept. Discrete notion having a single meaning. In a controlled vocabulary a concept is mapped to one or more of the words that convey its meaning.

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 Statement]

confidentiality. Prevention of disclosure to other than authorized individuals of a sponsor’s proprietary information or of a subject’s identity. [ICH E6 Glossary]

confirmatory trial. Phase 3 trial during which the previously revealed actions of a therapeutic intervention are confirmed. NOTE: Procedures in confirmatory trials should be set firmly in advance. *Compare to exploratory trial.*

conformity assessment. The process by which compliance with the

EMA’s Essential Requirements is assessed. See *also Notified Body*.

consent form. Document used during the informed 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. NOTE: The informed consent document provides a summary of a clinical trial (including its purpose, the treatment procedures and schedule, potential risks and benefits, alternatives to participation, etc.) and explains an individual’s rights as a subject. It is designed to begin the informed consent process, which consists of conversations between the subject and the research team. If the individual then decides to enter the trial, s/he gives her/his official consent by signing the document. *Synonym: informed consent form; see also informed consent.*

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 Glossary]

contingent subject trial contact. Planned response to an anticipated but conditional event in a clinical trial. [CDISC Trial Design Project]

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 E6 Glossary]

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 E6 Glossary]

control (of electronic records). To prepare and maintain case histories and other records for regulated clinical investigations. NOTE: Control is often used as a casual synonym for the terms in 21 CFR 312.62 requiring investigative sites to *prepare, maintain, and retain* adequate and accurate case histories.

control group. The group of subjects in a controlled study that receives no treatment, a standard treatment, or a placebo. [21 CFR 314.126] See *also controls*.

control(s). 1. Comparator against which the study treatment is evaluated [e.g., concurrent (placebo, no treatment, dose-response, active), and external (historical, published literature)] 2. Computer: processes or operations intended to ensure authenticity, integrity, and confidentiality of electronic records. NOTE: The protocol incorporates scientific rationale for selection of comparator and describes how the comparator serves as a reference point for the evaluation. [1. After ICH E10. 2. After 21 CFR Part 11; CSUCT]

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, active treatment, placebo, or dose comparison concurrent control. NOTE: For further information on “adequate and well-controlled study” see 21 CFR 314.126.

controlled terminology. Synonym for *controlled vocabulary*.

controlled vocabulary. A finite set of values that represent the only allowed values for a data item. These values may be codes, text, or numeric. See *also codelist*.

coordinating committee. A committee that a sponsor may organize to coordinate the conduct of a multicenter trial. [ICH E6]

coordinating investigator. An investigator assigned the responsibility for the coordination of investigators at different centers participating in a multicenter trial. [ICH E6]

correlation. The degree to which two or more variables are related. Typically the linear relationship is measured with either Pearson's correlation or Spearman's rho. NOTE: Correlation does not necessarily mean causation. [After HyperStat Online Glossary; ADaM]

covariate (prognostic). Factor or condition that influences outcome of a trial. [ADaM]

CRF data. Subset of clinical trial data that are entered into fields on a CRF.

CRF (paper). Case report form in which the data items are linked by the

physical properties of paper to particular pages. NOTE: Data are captured manually and any comments, notes, and signatures are also linked to those data items by writing or typescript on the paper pages. *See also eCRF, case report form.*

crossover trial. A trial design for which subjects function as their own control and are assigned to receive investigational product and controls in an order determined by randomizations, typically with a washout period between the two products. [Center for the Advancement of Clinical Research; ADaM]

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]

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

data and safety monitoring board (DSMB). *See data monitoring committee.*

data capture. *See data entry.*

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.

data clarification form. A form used to query an investigator and collect feedback to resolve questions regarding data.

data collection instrument. A substrate or tool (either electronic or paper) used to record, transcribe, or collect clinical data. [PR Project]

data element. 1. For XML, an item of data provided in a mark up mode to allow machine processing. 2. Smallest unit of information in a transaction. 3. A structured item characterized by a stem and response options together with a history of usage that can be standardized for research purposes across studies conducted by and for NIH. NOTE: The mark up or tagging facilitates document indexing, search and retrieval, and provides standard conventions for insertion of codes. [1. FDA - GL/IEEE. 2. Center for Advancement of Clinical Research. 3. NCI, caBIG]

data encryption standard (DES). A FIPS approved cryptographic algorithm for encrypting (enciphering) and decrypting (deciphering) binary coded information. Encrypting data converts it to an unintelligible form called cipher. Decrypting cipher converts the data back to its original form called plaintext. The standard specifies both enciphering and deciphering operations, which are based on a 64 bit binary number called a key. Unauthorized recipients of the cipher who know the algorithm but do not have the correct key cannot derive the original data algorithmically. NOTE: Data that is considered sensitive by the responsible authority or data that represents a high value should be cryptographically protected if it is vulnerable to unauthorized disclosure or undetected modification during transmission or while in storage. [from

Federal Information Processing Standards (FIPS) Publication 46-2]

data entry. Human input of data into a structured, computerized format using an interface such as a keyboard, pen-based tablet, or voice recognition. NOTE: Although data capture is often used synonymously, capture implies direct entry of original source data into an electronic record rather than transcription (entry) from paper source. *Contrast with data acquisition, electronic data capture; direct entry.*

data integrity. A dimension of data contributing to trustworthiness and pertaining to the systems and processes for data capture, correction, maintenance, transmission, and retention. Key elements of data integrity include security, privacy, access controls, a continuous pedigree from capture to archive, stability (of values, of attribution), protection against loss or destruction, ease of review by users responsible for data quality, proper operation and validation of systems, training of users. NOTE: In clinical research the FDA requires that data relied on to determine safety and efficacy of therapeutic interventions be trustworthy and establishes guidance and regulations concerning practices and system requirements needed to promote an acceptable level of data integrity. [FDA, CSUICI, IEEE]. *Compare with data quality.*

data integrity verification. Process of manually supervised verification of data for internal consistency.

data interchange. Transfer of information between two or more parties, which maintains the integrity of the contents of the data for the purpose intended. *See also interoperability.*

data item. A named component of a data element. Usually the smallest

component [ANSI]. *See also data model, data element.*

data management conventions. Procedures and policies for data management (e.g., documented procedure(s) for resolving self-evident changes). [ICH E6] *See self-evident change.*

data management. Tasks associated with the entry, transfer, and/or preparation of source data and derived items for entry into a clinical trial database. NOTE: Data management could include database creation, data entry, review, coding, data editing, data QC, locking, or archiving; it typically does not include source data capture.

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 clinical data are examined for completeness, consistency, and accuracy.

data monitoring committee (DMC). Group of individuals with pertinent expertise that reviews on a regular basis accumulating data from an ongoing clinical trial. The DMC advises the sponsor regarding the continuing safety of current participants and those yet to be recruited, as well as the continuing validity and scientific merit of the trial. NOTE: A DMC can stop a trial if it finds toxicities or if treatment is proved beneficial. [After FDA guidance on establishment and operation of clinical trial data monitoring committees]

data quality. A dimension of data contributing its trustworthiness and pertaining to accuracy, sensitivity,

validity, and suitability to purpose. Key elements of data quality include attributability, legibility (decipherable, unambiguous), contemporaneousness, originality (i.e., not duplicated), accuracy, precision, completeness, consistency (logical, not out of range). NOTE: Scientists may reasonably trust data that are accurate (high quality) that have also been reviewed by investigators and protected from unauthorized alteration (high integrity). *See also* ALCOA, *data integrity*.

data security. Degree to which data are protected from the risk of accidental or malicious alteration or destruction and from unauthorized access or disclosure. [FDA]

data selection criteria. The rules by which particular data are selected and/or transferred between the point of care and the patient record; subsequently, from the patient record to the database; and from database to inclusion in sub-population analyses.

data transformations. Algorithmic operations on data or data sets to achieve a meaningful set of derived data for analysis. [ADaM] *See also* *derived variable*.

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. 1. Checking data for correctness and/or compliance with applicable standards, rules, and conventions. 2. 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. [1. FDA. 2. ISO]

data listing. Set of observations organized by domain.

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

database lock. Action taken to prevent further changes to a clinical trial database. NOTE: Locking of a database is done after review, query resolution, and a determination has been made that the database is ready for analysis.

dataset. A collection of structured data in a single file. [CDISC, ODM, and SDS] *Compare with analysis dataset, tabulation dataset*.

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).

define.XML. Table used by XML review tools to configure a review engine to deal with CDISC standard data for a trial.

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.

dependent variable. Outcomes that are measured in an experiment and that are expected to change as a result of an experimental manipulation of the independent variable(s). [Center for Advancement of Clinical Research]

deployment. Readyng an electronic clinical trial system for field use by providing or disseminating capture devices, tokens, or passwords for users of an activated system. *See activation*.

derived variable. New variable created as a function of existing variables and/or application of mathematical functions. *See also variable, raw data*.

design. 1. In the context of clinical trials, *see design configuration*. 2. In the context of eClinical trials systems, a design for an application to support actions on electronic records.

design configuration. Clinical trial design developed to compare treatment groups in a clinical trial. NOTE: The configuration usually requires randomization to one or more treatment arms, each arm being allocated a different (or no) treatment. Examples include: Parallel Group Design, Crossover Design, Factorial Designs. [from ICH E9]

development plan. An ordered program of clinical trials, each with specific objectives. [Adapted from ICH E9, *see* ICH E8]. *See also clinical development plan*.

development process. *See drug development process*.

direct access. Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. NOTE: The 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 subjects' identities and sponsor's proprietary information. [ICH E6 Glossary]

direct entry. Recording of data by human or automated action where an electronic record is the original means of capturing the data into an electronic records system without a paper source document. Examples are an individual keying original observations into a system or the automatic recording into the system of the output from measuring devices such as a balance that measures subject's body weight or an ECG machine. *Compare with data entry, data acquisition.*

discontinuation. The act of concluding participation, prior to completion of all protocol-required elements, in a clinical study by an enrolled subject. NOTE: Four categories of discontinuation are distinguished: 1) dropout: active discontinuation by a subject [also a noun referring to such a discontinued subject]; 2) investigator-initiated discontinuation [e.g., subject experiences an unexpected adverse event]; 3) loss to follow-up: cessation of participation without notice by the subject and without ability to subsequently contact the subject to obtain further data; 4) sponsor-initiated discontinuation [e.g., change in protocol]. Note that subject discontinuation does not necessarily imply exclusion of subject data from analysis. "Termination" has a history of synonymous use, but is now considered non-standard. *See also withdrawal and ICH E3, Section 10.1 and FDA Guidance for Industry: Submission of Abbreviated Reports & Synopses in Support of Marketing Applications, IV A.*

discrepancy. The failure of a data point to pass a validation check. NOTE: Discrepancies may be detected by computerized edit checks or observed/identified by the data reviewer as a result of manual data review. *See also query.*

disease. Any deviation from or interruption of the normal structure or

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)

function of a part, organ, or system of the body as manifested by characteristic symptoms and signs. [Dorland's Medical Dictionary]

distribution. 1. In statistics, a group of ordered values; the frequencies or relative frequencies of all possible values of a characteristic. 2. In pharmacokinetics, the processes that control transfer of a drug from the site of measurement to its target and other tissues. [1. AMA Manual of Style]. *See also ADME.*

document (HL7). An ordered presentation of XML elements, possibly including text and tabular analyses, description, and figures. Descriptors for HL7 documents include type, class, and element. NOTE: In HL7, a document can be either physical (referring to the paper) or logical (referring to the content) with the following characteristics: 1) Stewardship; 2) Potential for authentication; 3) Wholeness; 4) Human readability; 5) Persistence; 6) Global vs. local context.

document root. The element in an XML document that contains all other

elements; the first element in the document. [SPL Glossary]

document type definition (DTD).

XML specification for content and presentation of data and text in a document including definitions for the elements considered to be legal in the document. NOTE: Agreeing on a common DTD facilitates interoperability among systems incorporating the agreed standards. [from XML files.com]

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 E6 Glossary]

domain. A collection of observations with a topic-specific commonality about each subject in a clinical investigation. NOTE: CDISC classifies domains. For example, the *Interventions* class is a domain that captures investigational treatments, therapeutic treatments, and surgical procedures that are intentionally administered to the subject (usually for therapeutic purposes) either as specified by the study protocol (e.g., exposure), coincident with the study assessment period (e.g., concomitant medications), or other substances self-administered by the subject (such as alcohol, tobacco, or caffeine). The *Events* class captures occurrences or incidents independent of planned study evaluations occurring during the trial (e.g., “adverse events” or “disposition”) or prior to the trial (e.g., “medical history”). The *Findings* class captures the observations resulting from planned evaluations such as observations made during a physical examination, laboratory tests, ECG testing, and sets of individual questions listed on questionnaires.

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. [Center for Advancement of Clinical Research]

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 Manual of Style]

dosage form. Physical characteristics of a drug product, (e.g., 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]. See also *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. [from Center for Advancement of Clinical Research]

dosage strength. 1. Proportion of active substance to excipient, measured in units of volume or concentration. 2. The strength of a drug product tells how much of the active ingredient is present in each dosage. [2. FDA Glossary of Terms]

dose. The amount of drug administered to a patient or test subject at one time or the total quantity administered. [AMA Manual of Style]

double-blind study. A study in which neither the subject nor the investigator nor the research team interacting with the subject or data during the trial 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 or observation required of him/her by the study protocol. [from ICH E9]

drug. 1. Article other than food intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; or intended to affect the structure or any function of the body. Not a device or a component, part, or accessory of a device. 2. Substance recognized by an official pharmacopoeia or formulary. [from FDA Glossary of Terms, CDER]

drug development process. The program for advancing an investigational product from preclinical studies through approval for marketing following review by regulatory agencies.

drug product. 1. A dosage form that contains an active drug ingredient or placebo. 2. A finished dosage form as described in regulations. [SPL Glossary]

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

eClinical trial. Clinical trial in which primarily electronic processes are used to plan, collect (acquire), access, exchange, and archive data required for conduct, management, analysis,

and reporting of the trial. *Synonyms:* *eClinical study, eClinical investigation.*

eCRF. 1. Auditable electronic record designed to capture information required by the clinical trial protocol to be reported to the sponsor on each trial subject. 2. 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. [FDA CSUCT]

eCRT. CRTs provided in electronic format for eSubmissions (electronic regulatory submissions). NOTE: According to FDA guidance, eCRTs are datasets provided as SAS Transport files with accompanying documentation in electronic submissions. 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. Becoming obsolete, being replaced by SDTM.

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. NOTE: Time-of-entry edit checks are a type of edit check that is run (executed) at the time data are first captured or transcribed to an electronic device at the time entry is completed of each field or group of fields on a form. Back-end edit checks are a type that is run against data that has been entered or captured electronically and has also been received by a centralized data store.

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] See also *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.

electronic data capture (EDC). The process of collecting clinical trial 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 with an audit trail. EDC usually denotes manual entry of *CRF data* by transcription from source documents. The transcription is typically done by personnel at investigative sites. See also *data entry, direct data entry, data acquisition.*

electronic health record (EHR). An electronic record for health care providers to create, import, store, and use clinical information for patient care, according to nationally recognized interoperability standards. NOTE: The EHR has the following distinguishing features: able to be obtained from multiple sources; shareable; interoperable; accessible to authorized parties. [After National Office of Health Information Technology—HIT, USHHS]

electronic medical record (EMR). An electronic record for health care providers within one healthcare organization to create, store, and use clinical information for patient care. An electronic record derived from a computerized system used primarily for delivering patient care in a clinical setting. NOTE: EMRs may serve as source documents, and such data could

serve also as source data for clinical trials provided that the controls on the EMR system and the transfer of such data to the eClinical trial system were to fulfill regulatory requirements (e.g., 21 CFR Part 11).

electronic personal health record (ePHR). An electronic record for individuals to create, import, store, and use clinical information to support their own health.

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 CSUCT; 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. [CSUCT Glossary; 21 CFR Part 11.3(7)]

element. 1. In trial design, a basic building block for time within a clinical trial comprising 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. PR Project. 2. HL7]

endpoint. Variable that pertains to the efficacy or safety evaluations of a trial. NOTE: Not all endpoints are themselves assessments since certain endpoints might apply to populations or emerge from analysis of results. That is, endpoints might be facts about assessments (e.g., prolongation of survival). See also *variable.*

enroll. To register or enter a subject into a clinical trial. NOTE: Once a subject has been enrolled, the clinical trial protocol applies to that subject.

enrollment. 1. The act of enrolling one or more subjects. 2. The class of enrolled subjects in a clinical trial.

enrollment (cumulative). Current enrollment as well as any ever-enrolled subjects who have ended participation.

enrollment (current). Subjects actively continuing to participate in a clinical trial as of the current date.

enrollment (target). 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.

Enterprise Vocabulary Services (EVS). A U.S. national resource to house and maintain a number of health-related glossaries and controlled vocabularies under strict versioning. NOTE: Includes the CDISC Glossary. [NCI]

epoch. Interval of time in the planned conduct of a study. An epoch is associated with a purpose (e.g., screening, randomization, treatment, follow-up), which applies across all arms of a study. NOTE: *Epoch* is intended as a standardized term to replace: *period*, *cycle*, *phase*, *stage*. See also *arm*, *visit*.

ePRO. PRO data initially captured electronically. NOTE: Usually ePRO data is captured as eSource. [DIA ePRO Working Group]. See also *patient reported outcome*, *PRO*, *eSource*.

equipoise. A state in which an investigator is uncertain about which arm of a clinical trial would be therapeutically superior for a patient.

NOTE: 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. NOTE: 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.

eSource. Source record that is electronic. See also *source*, *electronic record*.

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

eSource document. The electronic record used to aggregate a particular instance of eSource data items for capture, transmission, storage, and/or display, and serving as a *source document* for a clinical investigation. NOTE: Electronic source documents are recorded in electronic systems according to conventions (such as those for PDF documents) that ensure that all the fields of eSource data and associated contextual information (e.g., time of capture, time zone, authorship, signatures, revisions) are linked to each other in a particular structure for presentation. The encoded specifications in the electronic record thus serve the same role as have the physical properties of

paper (binding items together). eSource documents are subject to regulations and guidance that apply to source documents. See also *source documents*. [after eSDI, CDISC]

essential documents. Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. [ICH E6 Glossary]

established name. The official name of a drug substance. [Food, Drug, and Cosmetic Act]

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

ethnicity. Denotes social groups with a shared history, sense of identity, geography, and cultural roots.

European Medicines Agency (EMA). The regulatory agency for the EU.

evaluable (for efficacy and safety). Pertains to data or subjects that meet Statistical Analysis Plan criteria for inclusion in Efficacy/Safety datasets.

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 also *ADME*.

exploratory IND study. A clinical study that is conducted early in Phase 1; involves very limited human exposure and has no therapeutic or diagnostic intent (e.g., screening studies, microdose studies) [FDA Guidance for Industry, Investigators, and Reviewers: Exploratory IND Studies, January 2006] See also *Phase 0*.

exploratory study. Phase 1 or 2 study during which the actions of a

therapeutic intervention are assessed and measured. NOTE: Procedures in exploratory studies may appropriately be altered to expand the scope or method of investigation. *Compare to confirmatory study.*

extraction transformation load (ETL). A class of software applications for data extraction, transformation, and loading that are used to implement data interfaces between disparate database systems, often to populate data warehouses.

field. Locus on a data collection instrument (usually a CRF) for recording or displaying a data element. *See data item.*

File Transfer Protocol (FTP). A standard protocol for exchanging files between computers on the Internet. *See also 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. A meaningful interpretation of data or observations resulting from planned evaluations. *Compare to conclusion, hypothesis.*

first subject in (FSI, FPI). 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 will have signed an informed consent form. *Synonym: first patient in.*

first subject screened. First subject who signs the informed consent form

and is screened for potential enrollment and randomization into a study but has not yet been determined to meet the inclusion/exclusion criteria for the trial.

first subject treated. First subject who receives the test article or placebo in a clinical investigation.

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

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

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

Form. A collection of items and item groups for capturing and displaying clinical trial data.

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. Status of a database, file, or element that has been presumed to be in its final state pending “lock” and where further editing is prevented without “unfreezing.” NOTE: Freezing and unfreezing are usually formalized in audit trails and differ from “locking” and “unlocking” only in the degree of approval required. See *database lock*.

functional roles (in a study).
See *role*.

gender. Subject self-identification re: masculine/feminine. [IOM] See *also sex*.

generalizability. 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.

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 words or 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. 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. [ICH]

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

granularity. Refers to the size of an information unit in relation to a whole. NOTE: Structuring “privileges” in electronic systems is said to be highly granular when each of many roles can differ in their capacity to act on electronic records.

group sequential design. A trial design that allows a look at the data at particular time points or after a defined number of patients have been entered and followed up based on formulating a stopping rule derived from repeated significance tests. [Center for Advancement of Clinical Research]

handwritten signature. The scripted name or legal mark of an individual handwritten by that individual and executed or adopted with the present intention to authenticate a writing in a permanent form. NOTE: The act of signing with a writing or marking instrument such as a pen or stylus is preserved. [21CFR 11]

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 authority. *Synonym for regulatory authority.* NOTE: Used in the European Union.

Health Level 7 (HL7). An ANSI-accredited Standards Developing

Organization (SDO) operating in the healthcare arena. 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.

healthcare provider. 1. One who directly or indirectly administers interventions that are designed to improve the physical or emotional status of patients. 2. A person licensed, certified, or otherwise authorized or permitted by law to administer healthcare in the ordinary course of business or practice of a profession, including a healthcare facility. [1. PR Project. 2. HL7]

healthy volunteer. Subject (not a patient) in a clinical trial. NOTE: Usually healthy volunteers serve as subjects in Phase 1 trials.

human subject. 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. [21 CFR 50.3]. *Synonym: subject/trial subject.*

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

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

hypertext. Links in a document that permit browsers to jump immediately to another document. NOTE: In most

browsers links are displayed as colored, underlined text.

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 Statement]

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

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

independent data monitoring committee (IDMC). 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] *See also data monitoring committee.*

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. NOTE: The legal status, composition, function, operations, and regulatory requirements pertaining to independent ethics committees may differ among countries but should allow the independent ethics committee to act in agreement with GCP as described in the ICH guideline. [ICH] *See also institutional review board.*

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

informed consent. An ongoing process that provides the subject with explanations that will help in making educated decisions about whether to begin or continue participating in a trial. Informed consent is an ongoing, interactive process rather than a one-time information session. NOTE: Under 21 CFR 50.20, no informed consent form 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." [ICH] *See also consent form.*

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

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

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

institutional review board (IRB). An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. [ICH E6 1.31] *Synonyms: independent review board, independent ethics committee, committee for the protection of human subjects.*

instrument. A means to capture data (e.g., questionnaire, diary) plus all the information and documentation that supports its use. NOTE: Generally, instruments include clearly defined methods and instructions for administration or responding, a standard format for data collection, and well-documented methods for scoring, analysis, and interpretation of results. [from PRO Draft Guidance] *Compare to questionnaire, survey (see Comments on Draft PRO Guidance, April 4, 2006, by ISOQoL, p. 8).*

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. NOTE: This has the consequence that subjects allocated to a treatment group should be followed up, assessed, and analyzed as members of that group irrespective

of their compliance with the planned course of treatment. The principle is intended to prevent bias caused by loss of participants that may reflect non-adherence to the protocol and disrupt baseline equivalence established by random assignment. [ICH E9; after CONSORT Statement]

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 center). 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.

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

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. Pertaining to data that do not include contradictions.

Internet. A global system of computer networks that provides the common TCP IP infrastructure for email, the World Wide Web, and other online activities.

Internet service provider (ISP). A company that provides access to the Internet for individuals and organizations.

interoperability. Ability of two or more systems or components to exchange information and to use the information that has been exchanged.

[IEEE Standard Computer Dictionary].
See also *syntactic, semantic*.

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 study that is believed to have an effect on outcomes of interest in a study (e.g., health-related quality of life, efficacy, safety, pharmacoeconomics).
Synonyms: therapeutic intervention, medical product. See also: test articles; devices; drug product; medicinal product; combination product.

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

investigational treatment. An intervention under investigation in a clinical study.

investigator. An individual who actually conducts a clinical investigation (i.e., 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). [21 CFR 50.3] See also *sponsor-investigator, site 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 non-clinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.

item. 1. A representation of a clinical variable, fact, concept, or instruction in a manner suitable for communication, interpretation, or processing by humans or by automated means. NOTE: Items are collected together to form item groups. 2. An individual question, statement, or task that is evaluated by the patient to address a particular concept to be measured by a PRO instrument. [1. CDISC. 2. from PRO Draft Guidance] See also *response option*.

item definition. 1. In a questionnaire or form to be completed in a clinical trial, the specification of a question and the specification of the format and semantics of the response. 2. Formal specification of the properties of an item or field of data in an eClinical trial. [2. ODM]

item generation. Establishing the content to be covered by the items in a PRO instrument, including generating item wording, evaluating the completeness of item coverage of the concepts of interest, and performing initial assessment of clarity and readability. NOTE: PRO instrument item generation is potentially incomplete without patient involvement. [from ISOQOL comments on PRO Draft Guidance]

item group definition. The specification in an eClinical trial of a collection of items often clinically related to each other and useful to consider as an ensemble. NOTE: Item groups are likely to have greater granularity in analysis datasets using SDTM which can, for example, distinguish between different therapy types: study therapy, prior therapy, concomitant therapy, protocol forbidden therapies, rescue therapies. [ODM]

Janus. 1. A logical design conceived by the FDA for a data warehouse intended to integrate submission data, protocol descriptions, and analysis plans from clinical and animal studies into an FDA review environment that uses a set of validated, standards-based tools to allow reproducible cross-study, data mining, and retrospective comparative analysis. 2. The name assigned to a component of the NCI's caBIG Clinical Research Information Exchange (CRIX) initiative, representing a joint NCI/FDA project to develop a physical implementation of the Janus model. NOTE: Sometimes written as JANUS, the term is not an acronym, but harkens to the Roman god of gates and doors, beginnings and endings.

label. Description of a drug product/device that includes: the indication, who should use it, adverse events, instructions for use, and safety information. NOTE: Labels must be approved by regulatory authorities. [FDA; SPL] *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., 21 CFR 201.56 and 201.57 for human prescription drugs; 201.66 for human over-the-counter drugs; 21 CFR 801 for medical devices; and 21 CFR 606.122 for blood products). *See also structured product label.*

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

last subject out/complete (LSC/LPC or LSO/LPO). 1. The date and time when the last subject has reached a planned or achieved milestone representing the completion of the trial. 2. The last subject to complete a trial. *See also subject, patient, completion.*

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

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, E6 Glossary]

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

life-threatening adverse event/experience. Any adverse drug experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred (i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death). [FDA 21 CFR §312.32; ICH-E2A]

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).

mapping. In the context of representing or exchanging data, connecting an item or symbol to a code or concept. *Compare with translation.*

marketing support trials. Clinical studies that are designed to clarify therapeutic benefits of a marketed product or to show potential decision-makers the rationale for preferring one therapy over another.

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

masking. *See blinding.*

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

matching. *See pairing.*

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

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

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

medical product. *See intervention.*

medicinal product. *Synonym for therapeutic intervention, but usually a drug.*

Medicines and Healthcare products Regulatory Agency (MHRA). The UK government agency responsible for ensuring that medicines and medical devices work, and are acceptably safe. [MHRA]

mega-trials. Massive clinical trials that test the advantages of therapeutic interventions by enrolling 10,000 or more subjects. *Synonym: large sample trials.*

Memorandum of Understanding (MOU). A formal agreement between the Food and Drug Administration (FDA) and federal, state, or local government agencies; academic institutions; and other entities. NOTE: The MOU constitutes an understanding between the parties but is a non-binding agreement. It is FDA's policy to enter into MOUs with other entities whenever there is a need to define lines of authority or responsibility, or to clarify cooperative procedures.

message (HL7). The atomic unit of data transferred between systems. It comprises a group of segments in a defined sequence. Each message has a message type that defines its purpose. 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. [HL7]

meta-analysis. The formal evaluation of the quantitative evidence from two or more trials bearing on the same question. NOTE: This most commonly involves the statistical combination of summary statistics from the various trials, but the term is sometimes also used to refer to the combination of the raw data. [from ICH E9 Glossary]

metabolism. The biochemical alteration of substances introduced into the body.

metadata. Data that describe other data, particularly XML tags characterizing attributes of values in clinical data fields.

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]

missing data. 1. Data not completed or corrupted in reports and case report forms. 2. Particularly the data not captured when a subject withdraws from a trial. NOTE: Reviewers are concerned about missing data (meaning 2) since patients who are not improved or who believe they have experienced side effects may be particularly prone to leave a trial, thus skewing the analysis of results if such analysis were to be done only on the subjects who had continued with the trial. Trial designs therefore specify plans for how such missing data will be treated in analysis. *See also intention to treat.*

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

model. A formal structure for representing and analyzing a process such as a clinical trial or the information pertaining to a restricted context (e.g., clinical trial data). [CDISC]

modem. From modulator/demodulator; a device that converts 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 and GCP guidance. NOTE: 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. [from ICH E6, 5.18] *See also clinical research associate.*

monitoring. The act of overseeing the progress of a clinical trial and of ensuring that it is conducted, recorded,

and reported in accordance with the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [ICH E6 Glossary]

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. [from ICH E6, 5.18]

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.*

natural language. Language as used in ordinary communications among humans and distinguished from controlled terminologies and structured languages used exclusively for communication and interoperability among machines.

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 the order of experimental and control treatments randomized.

nomenclature. Application of naming conventions. *Compare with vocabulary, terminology.*

nonclinical study. Biomedical studies not performed on human subjects. [ICH E6 Glossary]

not approvable letter. An official communication from FDA to inform a sponsor of a marketing application that the important deficiencies described in the letter 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. 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. NOTE: 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, and is used because most statistical methods are less able to prove something true than to provide strong evidence that it is false. The assertion that no true association or difference in the study outcome or comparison of interest between comparison groups exists in the larger population from which the study samples are obtained. *See also research hypothesis.* [from AMA Manual of Style]

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

objective. The reason for performing a trial in terms of the scientific questions to be answered by the analysis of data collected during the trial. 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 level that is obtained by a measuring device rather than a human judgment or assessment. *See also 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. 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 also variable.* Referring to an ad hoc comment as an observation is colloquial. [1. CONSORT Statement. 2. SDTM]

observer assessment. An assessment of patient condition made by an observer (investigator, nurse, clinician, family member, etc.). 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 making an observer assessment. *Compare to PRO, proxy assessment.*

ontology. An explicit formal specification of how to represent relationships among objects, concepts, and other entities that belong to a particular domain of experience or knowledge. *See also terminology.*

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

open to enrollment. The status of a study such that a subject can be enrolled into that study. NOTE: Registry terminology in common use is "open to recruitment"; however, recruitment can begin upon IRB approval of the site; whereas enrollment requires availability of study supplies, subject informed consent, etc., to allow participation of eligible subjects.

operational model. The set of CDISC data standards (including ODM and LAB) used to capture and archive data from clinical trials.

opinion (in relation to independent ethics committee). The judgment and/or the advice provided by an independent ethics committee. [ICH E6 Glossary]

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.). [1. CONSORT Statement. 2. from SDTM for descriptions of the Define document]

original data. The first recorded study data values. NOTE: FDA is allowing original documents and the original data recorded on those

documents to be replaced by copies provided that the copies have been verified as identical in content and meaning. (See FDA Compliance Policy Guide 7150.13). [Modified from CSUICI] *See also certified copy, source.*

outcome (of adverse event).

Refers to the resolution of an adverse event. 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. [SDTM Events class of observation]

outcome. 1. 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. 2. (SDTM) The result of carrying out a mathematical or statistical procedure. NOTE: 1. Such events and experiences are called clinical outcomes independently of whether they are part of the original question/protocol of the investigation. [1. Guyatt, G., Schunemann H., Dept. Epidemiology & Statistics, McMaster University—personal communication] *See also variable; outcome can be a result of analysis; outcome is more general than endpoint in that it does not necessarily relate to a planned objective of the study.*

outcomes research. Research concerned with benefits, financial costs, healthcare system usage, risks, and quality of life as well as their relation to therapeutic interventions. NOTE: Usually distinguished from research conducted solely to determine efficacy and safety. [Guyatt et al., 1993] *See also pharmacoeconomics, quality of life.*

outliers. Values outside of an expected range.

packaging. The material, both physical and informational, that

contains or accompanies a marketed or investigational therapeutic agent once it is fully prepared for release to patients and/or subjects in clinical trials.

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

parallel trial. Subjects are randomized to one of two or more 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). 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. Parameters are rarely known and are usually estimated by statistical computation from samples. Thus the term is narrower than variable. [Parexel Barnett; ADaM; HyperStat Online] *See also variable, outcome.*

participant. A person or entity with a role in healthcare or a clinical study. NOTE: Participants in a clinical trial may include subjects and study personnel. A subject participates as part of the group of people who are administered the therapeutic intervention or control. *See also subject, patient.*

password aging. A practice applying to multi-user computer systems where the validity of a password expires after a certain pre-set

period. NOTE: FDA requires that passwords that are part of electronic signatures be “periodically checked, recalled or revised,” but does not mandate password aging. [After NIST, 21 CFR Part 11]

patient. Person under a physician’s care for a particular disease or condition. NOTE: A subject in a clinical trial is not necessarily a patient, but a patient in a clinical trial is a subject. *See also subject, trial subject, healthy volunteer. Although often used interchangeably as a synonym for subject, a healthy volunteer is not a patient.*

patient file. One that contains demographic, medical, and treatment information about a patient or subject. It may be paper- or computer-based or a mixture of computer and paper records.

patient-reported outcome (PRO). Information 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. NOTE: PROs are used to assess outcomes involving the patients’/subjects’ perceptions, symptoms, satisfaction with treatment, adherence to prescribed regimens. 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. A PRO is usually a subjective assessment of feeling or function distinguished from a self-reported objective measurement such as body weight. [from PRO Draft Guidance, Gordon Guyatt and Holger Schunemann—personal communication; Patrick, D.L., 2003. After Acquardo C., Berzon C., et al., 2001] *Synonym: subject-reported outcome (SRO). See also outcome, subject, patient, instrument.*

performed activity. Clinical trial events as they actually occurred

(as compared with events planned in the protocol).

permissible values. Limited universe of options for data items. (e.g., drop-down menus, codelists, pick lists).

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]

period effect. An effect occurring during a period of a trial in which subjects are observed and no treatment is administered.

permanent data. Data that become or are intended to become part of an electronic record in relation to a regulatory submission. NOTE: Any changes made to such permanent data are recorded via an audit trail so that prior values are not obscured.

pharmacodynamics. Branch of pharmacology that studies reactions between drugs and living structures, including the physiological responses to pharmacological, biochemical, physiological, and therapeutic agents.

pharmacoeconomics. Branch of economics that applies cost-benefit, cost-utility, cost-minimization, and cost-effectiveness analyses to assess the utility 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 study of genetic response to a drug.

pharmacogenomic test. An assay intended to study interindividual variations in wholegenome 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 respond favorably, adversely, or not at all to an investigational product.

pharmacokinetics. Study of the processes of bodily absorption, distribution, metabolism, and excretion (ADME) of medicinal products.

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.

phase. One in a set of successive stages in a progression or sequence such as 1. a step in the progression of a therapy from initial experimental use in humans to postmarket evaluation. 2. a stage in the conduct of a clinical trial. NOTE: Clinical trials are generally categorized into four (sometimes five) phases. A therapeutic intervention may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases. *For meaning 1, see Phase 0–5. For meaning 2, see epoch.*

Phase 0. First-in-human trials, in a small number of subjects, that are conducted before Phase 1 trials and

are intended to assess new candidate therapeutic and imaging agents. The study agent is administered at a low dose for a limited time, and there is no therapeutic or diagnostic intent. NOTE: FDA Guidance for Industry, Investigators, and Reviewers: Exploratory IND Studies, January 2006 classifies such studies as Phase 1. [Improving the Quality of Cancer Clinical Trials: Workshop Summary—Proceedings of the National Cancer Policy Forum Workshop, Improving the Quality of Cancer Clinical Trials (Washington, DC, Oct 2007)]

Phase 1. The initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. 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 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80. Phase 1 studies also include studies of drug metabolism, structure–activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. [After FDA CDER Handbook, ICH E8]

Phase 2. Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the

drug. NOTE: Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects. [After FDA CDER Handbook, ICH E8]

Phase 2A. Controlled clinical studies that occur after the completion of Phase 1 studies and the first set of exposure-response studies in patients, and before beginning Phase 2B (i.e., patient dose-ranging trial) and Phase 3 clinical efficacy-safety studies. [FDA draft Guidance for Industry End of Phase 2A meetings, 9/08].

Phase 3. Studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained and are intended to gather the additional information about effectiveness and safety that is needed to confirm efficacy and evaluate the overall benefit–risk relationship of the drug and to provide an adequate basis for physician labeling. NOTE: Phase 3 studies usually include from several hundred to several thousand subjects. [After FDA CDER Handbook, ICH E8]

Phase 3B. A subcategory of Phase 3 trials done near the time of approval to elicit additional findings. NOTE: Dossier review may continue while associated Phase 3B trials are conducted. These trials may be required as a condition of regulatory authority approval.

Phase 4. Postmarketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use that may be requested by regulatory authorities in conjunction with marketing approval. NOTE: These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in

Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time. [After FDA CDER Handbook, ICH E8]

Phase 5. Postmarketing surveillance is sometimes referred to as Phase 5. See *also outcomes research*.

placebo. A pharmaceutical preparation that does not contain the investigational agent. In blinded studies, it is generally prepared to be physically indistinguishable from the preparation containing the investigational 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 Style Manual]

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

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

preamble. A section preceding the text of a final FDA regulation published in the Federal Register. NOTE: "The preamble is to contain a thorough and comprehensible explanation of the reasons for the Commissioner's decision on each issue" raised in comments submitted in response to the proposed regulation. [from 21CFR10.40]

preclinical studies. Animal studies that support Phase 1 safety and tolerance studies and must comply with good laboratory practice (GLP). NOTE: Data about a drug's activities

and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical studies or trials).

Pre-Market Approval Application (PMA). An application to FDA for a license to market a new device in the United States.

primary objective. The primary objective(s) 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). [ICH E6 6.3] See *also objective*.

primary variable. An outcome variable specified in the protocol to be of greatest importance to the primary objective of the trial, usually the one used in the sample size calculation. NOTE: Differences between groups in the primary and secondary variable(s) are believed to be the result of the group-specific interventions. [PR Project; CONSORT Statement] *Synonyms: primary endpoint, outcome.* See *also primary objective*.

product. 1. Drug product: A finished dosage form that contains a drug substance. 2. A physical entity that is intended to diagnose, treat, or prevent a disease or other abnormal condition and subject to regulatory authority. [Modified from FDA Glossary of Terms]

PROMIS. NIH-sponsored project for the development and evaluation of PRO item banks and computer adaptive testing for pain, fatigue, physical function, social function, and emotional well-being. [NIH]

proprietary name. A commercial name granted by a naming authority for use in marketing a drug/device product. [SPL] *Synonyms: trade name, brand name.*

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

protocol. A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments. NOTE: Present usage can refer to any of three distinct entities: 1) the plan (i.e., content) of a protocol, 2) the protocol document, and 3) a series of tests or treatments (as in oncology). [ICH E6 Glossary]

protocol amendment(s). A written description of a change(s) to or formal clarification of a protocol. [ICH E3]

protocol approval (Sponsor). Sponsor action at the completion of protocol development that is marked when the signature of the last reviewer on the protocol approval form has been obtained, signifying that all reviewer changes to the protocol have been incorporated. NOTE: Approval by the sponsor usually initiates secondary approvals by IRBs, regulatory authorities, and sites. Protocol amendments usually also require a cycle of approval by sponsor and study staff prior to taking effect.

protocol deviation. A variation from processes or procedures defined in a protocol. Deviations usually do not preclude the overall evaluability of subject data for either efficacy or safety, and are often acknowledged and accepted in advance by the sponsor. NOTE: Good clinical practice recommends that deviations be summarized by site and by category as part of the report of study results so that the possible importance of the

deviations to the findings of the study can be assessed. *Compare to protocol violation.* [See ICH E3]

Protocol Identifying Number. Any of one or more unique codes that refers to a specific protocol. NOTE: There may be multiple numbers (Nat'l number, coop group number). [PR Project; eudraCT]

protocol referenced documents. Protocol referenced documents that optionally supplement the ICH GCP recommended sections of a protocol giving background information and rationale for the trial. [from ICH E6 1.44] *See also protocol.*

protocol title. Three categories of protocol title have evolved to address distinct standardized use cases. 1) Scientific Title: A comprehensive summary of study design and objectives, aimed at scientific audience. 2) Public Title: A brief description intended for the lay public in easily understood language. 3) Trial Acronym: Brief popular identifier. NOTE: The scientific title should include the trial acronym, if applicable [WHO http://www.who.int/ictrp/data_set/en/index1.html]. Scientific title may also be referred to as "official title." Public title may also be referred to as "brief title."

protocol violation. A significant departure from processes or procedures that were required by the protocol. Violations often result in data that are not deemed evaluable for a per-protocol analysis, and may require that the subject(s) who violate the protocol be discontinued from the study. *Compare to protocol deviation.*

proxy (as an origin of outcome measures). A proposed standardized qualifier variable to describe the origin of observations of the Findings class resulting from outcomes measures. Proxy describes outcome data

furnished by someone other than the patient and distinguishes the origin of the outcome from a self-report (PRO) directly from the patient. NOTE: The term proxy helps qualify outcomes measures that record feelings and symptoms reported by the patient but not recorded directly. [CDISC (extension of SDTM based on Table 2 Patrick, D.L., 2003)] *See also observer assessment.*

proxy respondent. Someone other than the patient who is responding about the patient on behalf of the patient, not as an observer. [Patrick, D.L., 2003; DIA ePRO Workgroup] *Compare to observer assessment.*

psychometric reliability. *See reliability, psychometric.*

psychometric validation. The specialized process of validating questionnaires used in outcomes research to show that they measure what they purport to measure. NOTE: Several types of validity are distinguished. For example, face validity means that an assessment instrument appears by inspection and consideration of the semantic content of items in it to be measuring what it is supposed to measure. Construct validity means that a scale based on one or more items measures an unobservable psychological construct (e.g., "distress") that it is proposed to measure. Construct validity is usually tested by measuring the correlation in assessments obtained from several scales purported to measure the same construct. [Guyatt et al., 1993; DIA ePRO Workgroup] *See also validation; compare to psychometric reliability.*

psychometrics. The science of assessing the measurement characteristics of scales that assess human psychological characteristics.

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 Statement]

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

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

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

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. NOTE: Quality of Life is one way to measure the benefits or negative impacts of an "improvement" measured in terms of a physiological or psychological symptom. QOL research seeks to quantify what an intervention means to a patient's sense that their life has changed. [WHO Group, 1994]

quantitative variable. One that can be measured and reported numerically to reflect a quantity or amount, ideally on a continuum.

query. A request for clarification on a data item collected for a clinical trial; specifically a request from a sponsor or

sponsor's representative to an investigator to resolve an error or inconsistency discovered during data review.

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 usually based on information contained in a data clarification.

questionnaire. A set of questions or items shown to a respondent in order to get answers for research purposes. [PRO Draft Guidance] See also *instrument, survey*.

random allocation. Assignment of subjects to treatment (or control) groups in an unpredictable way. NOTE: In a blinded study, 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. 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. [ICH E6 1.48] See also *balanced study*.

raw data. Data as originally collected. Distinct from derived. Raw data includes

records of original observations, measurements, and activities (such as laboratory notes, evaluations, data recorded by automated instruments) without conclusions or interpretations. Researcher's records of subjects/patients, such as patient medical charts, hospital records, X-rays, and attending physician's notes. NOTE: These records may or may not accompany an application to a Regulatory Authority, but must be kept in the researcher's file. See also *eSource, source data, source documents*.

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

reconstruction (of a study). For eClinical trials FDA expects archival trial records to support review of the data as well as the processes used for obtaining and managing the data so that the trustworthiness of results obtained can be evaluated. NOTE: Reconstruction from records should support evaluation of the operation and validity of computerized systems and the conformance of the systems to applicable regulations during design and execution of the trial as well as during the period of record retention. [from CSUCT VI D, 21 CFR Parts 11, 312]

recruitment (investigators). Process used by sponsors to identify, select, and arrange for investigators to serve in a clinical study.

recruitment (subjects). Process used by investigators to find and 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]

registry. A data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions. NOTE: The registry should contain basic information about each trial sufficient to inform interested subjects (and their healthcare practitioners) how to enroll in the trial. [FDAMA 113]

regulatory authorities. Bodies having the power to regulate. NOTE: 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. The degree to which a psychometric “instrument” is free from random error either by testing the homogeneity of content on multi-item tests with internal consistency evaluation or testing the degree to which the instrument yields stable scores over time. NOTE: Reliability pertains to questions concerning whether an instrument is accurate, repeatable, sensitive. Reliability is distinguished from validation, which answers whether the instrument (e.g., questionnaire) actually measure the selected “construct” (latent variable). For example a balance (scale) is easily understood as a possibly valid instrument to measure body weight. Its reliability would be assessed by measuring the sensitivity, repeatability and accuracy of the balance. The validity of using the balance for a

particular purpose could then be established by comparing the measured reliability to the reliability required for that purpose. [After Patrick, D.L., 2003] *Compare to psychometric validation; see also validation; instrument.*

repeat rule. Guide for repeating activities specified in protocol, including such features as the number of cycles and the criteria for stopping.

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

representative. *See legally acceptable representative.*

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

response option. One of several choices to be available for selection in response to a prompt, question or instruction (i.e., a *stem*) in a PRO item. *See also common data element, stem.*

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. NOTE: Retrospective capture is important in PROs 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. NOTE: 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 troubling side effects. However, the possibility of 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. HL7. 2. SDTM] *See also 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. 1. A subset of a larger population, selected for investigation to draw conclusions or make estimates about the larger population. 2. The number of subjects in a clinical trial. 3. Number of subjects required for primary analysis.

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

schedule of activities. A standardized representation of planned clinical trial activities including interventions (e.g., administering drug, surgery) and study administrative activities (e.g., obtaining informed consent, distributing clinical trial material and diaries, randomization) as well as assessments. *See also schedule of assessments.*

schedule of assessments. A tabular representation of planned protocol events and activities, in sequence. [after E3 Annexes IIIa and IIIb] *Synonym: flow chart. Compare to study design schematic.*

screen failure. Potential subject who did not meet one or more criteria required for participation in a trial. *See also screening of subjects.*

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

screening (of 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. *See also screen failure.*

screening trials. Trials conducted to detect persons with early, mild, and asymptomatic disease.

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

secondary objective. *See objective.*

secondary sponsor. Additional individuals, organizations or other legal persons, if any, that have agreed with the primary sponsor to take on responsibilities of sponsorship. [WHO, CTR Item 6]

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 Statement] *See also 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 known to be a male and a date of last pregnancy is provided). *See also discrepancy.*

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 also adverse experience.*

serious adverse experience. Any experience that suggests a significant hazard, contra-indication, side effect or precaution. *See also serious adverse event.*

server. A computer that controls a central repository of data, files, and/or applications that can be accessed and/or manipulated in some manner by client computers. A file server hosts files for use by client machines. An application server runs programs that may process and display data exchanged with client machines. After the arrival of the Web, server often refers to software and computers that perform database queries and collect and present timely data to users running browsers or other client applications.

sex. Phenotypic expression of chromosomal makeup that defines a study subject as male, female, or other. *Compare to gender.*

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

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

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

site. *See trial site.*

site 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 E6 1.35. 2.] *See also investigator.*

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. 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). 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; 21 CFR 11.10(a); ISO 9000-3; Huber, L. (1999) *See also validation, verification. Verification usually concerns confirmation that specified requirements have been met, but typically refers to the tracing of requirements and evidence of conformance in the individual phases or modules rather than suitability of the complete product. Validation is, “the evaluation of software at the end of the software development process to ensure compliance with the user requirements” (ANSI/ASQC A3-1978) and should not be thought of as an “end-to-end” verification.*

source. 1. The specific permanent record(s) upon which a user will rely for the reconstruction and evaluation of a clinical investigation. 2. Sometimes used as shorthand for source documents and/or source data. NOTE: Accuracy, suitability, and trustworthiness are not defining attributes of “source.” The term identifies records planned

(designated by the protocol) or referenced as the ones that provide the information underlying the analyses and findings of a clinical investigation. [After ICH E6, CSUIC] *See also original data, certified copy*

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 E6; CSUCT]

source data verification. The process of ensuring that data that have been derived from source data accurately represent the source data.

source document verification. The process by which the information reported by an investigator is compared with the source records or original records to ensure that it is complete, accurate, and valid. [Schuyll and Engel, 1999; Khosla et al., Indian J. Pharm 32:180-186, 2000] *Synonym: SDV. See also 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 medicotechnical departments involved in the clinical trial). *See also eSource document, source, original data, certified copy.* [ICH; CSUIC]

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]

sponsor. 1. An individual, company, institution, or organization that takes responsibility for the initiation and management of a clinical trial, although may or may not be the main funding organization. If there is also a secondary sponsor, this entity would be considered the primary sponsor. 2. A corporation or agency whose employees conduct the investigation is considered a sponsor and the employees are considered investigators. [1. After ICH E6 and WHO. 2. 21 CFR 50.3 (e)] *See also secondary sponsor.*

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. NOTE: The term does not include any person other than an individual (i.e., 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. [21 CFR 50.3f] [ICH]

standard. Criterion or specification established by authority or consensus for 1. measuring performance or quality; 2. specifying conventions that support interchange of common materials and information. NOTE: CDISC standards exist to support the exchange of clinical data, for example, at both the *syntactic* and *semantic* levels. *See interoperability.*

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.

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 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 method. The particular mathematical tests and techniques that are to be used to evaluate the clinical data in a trial. [ICH E9; from the Center for Advancement of Clinical Research]

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 when the null hypothesis is true there is only a 1 in 20 chance of rejecting it.

stem. The prompt, question, or instruction in a PRO item. *See also response option, item.*

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]

structured product label (SPL). The Structured Product Labeling (SPL) specification is an HL7 ANSI-approved document markup standard that specifies the structure and semantics for the exchange of product information. [HL7]

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

study coordinator. *See clinical research coordinator.*

study description. Representation of key elements of study (e.g., 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) [Modified from Pocock, *Clinical Trials: A Practical Approach*] *See Trial Design Model. See also, arm, epoch, and visit.*

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

study design schematic. Schematic diagram (not tabular) of study design, procedures, and stages. [example: ICH E3 Annexes IIIa and IIIb] *Compare to schedule of assessments.*

study initiation date. Date and time of first subject enrollment into a study, as verifiable by a convention that is consistent with authoritative

regulatory criteria. [modified from ICH E3] Compare with *study start*. *Synonym: date of first enrollment.*

study population. Defined by protocol inclusion/exclusion criteria.

study protocol. *See protocol.*

study start. The formal recognition of the beginning of a clinical trial that is referred to in the clinical study report.

study treatment. *See investigational intervention.*

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

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

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

subject trial contact. Any activity, anticipated in the study protocol, involving a subject and pertaining to collection of data. *See visit.*

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

subject-reported outcome (SRO).

An outcome reported directly by a subject in a clinical trial. [Patrick, D.L., 2003] *See also patient-reported outcome (PRO).*

submission model. A set of data standards (including SDTM, ADaM, and define.xml) for representing data that are submitted to regulatory authorities to support product marketing applications. NOTE: CDISC submission data consist of: tabulations that represent the essential data collected about patients; analysis data structured to support analysis and interpretation; and metadata descriptions.

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]

supporting variables. *See variable.* [FDA Drug Review Glossary]

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

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

survey. Any means (e.g., questionnaire, diary, interview script, group of items) that is used to collect PRO data. NOTE: Survey refers to the content of the group of items and does not necessarily include the training and scoring documents generally not seen by respondents. [from ISOQOL

comments on PRO Guidance] *Compare to instrument.*

synopsis. Brief overview prepared at the conclusion of a study as a routine part of a regulatory submission, summarizing the study plan and results; includes numerical summary of efficacy and safety results, study objective, criteria for inclusion, methodology, etc. [after ICH E3]

syntactic. The order, format, content of clinical trial data and/or documents as distinct from their 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. *See also semantic, semantic interoperability.*

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

table of roles and responsibilities.

A cumulative record documenting operational access and authorizations of study personnel to electronic systems used in eClinical trials.

tabulation dataset. A dataset structured in a tabular format. NOTE: The CDISC Study Data Tabulation Model (SDTM) defines standards for tabulation datasets that fulfill FDA requirements for submitting clinical trial data.

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.

target study population.

Demographic and health condition of the population to be included in a clinical study.

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. *Synonym: vendor.*

term. One or more words designating something. NOTE: In a controlled vocabulary, terms are considered to refer to an underlying *concept* having a single meaning. Concepts may be linked to several synonymous terms.

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

termination (of trial). Premature discontinuation of a trial prior to plan. [EU Clinical Trial Directive]

terminology. 1. Set of concepts, designations, and relationships for a specialized subject area. *See Glossary.* 2. In the context of clinical research in human subjects, a standardized, finite set of terms (e.g., picklists, MedDRA codes) that denote patient findings, circumstances, events, and interventions. *Compare with glossary, which is a list of words and their definitions pertaining to usage in a particular field or context. Often used synonymously with vocabulary. Contrast with nomenclature.*

therapeutic intervention. *See intervention.*

token. Physical key that provides access to a secure electronic system or location.

transcription. Process of transforming dictated or otherwise documented

information from one storage medium to another. NOTE: often refers explicitly to data that is manually transcribed from source docs or measuring devices to CRFs or to eCRFs.

transition rule. A guide that governs the allocation of subjects to operational options at a discrete decision point or branch (e.g., assignment to a particular *arm*, *discontinuation*) within a clinical trial plan. See *branch*.

translation. Converting information from one natural language to another while preserving meaning. Compare with *mapping*.

transmit. To transfer data, usually electronically. NOTE: In eClinical investigations data are commonly transmitted from subjects to clinical study sites, within or among clinical study sites, contract research organizations, data management centers, and sponsors, or to regulatory authorities. [modified from CSUIC].

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, arms epochs, visits; suitable also for syntactic interpretation by machines. [CDISC] See *study design*.

trial monitoring. Oversight of quality of study conduct and statistical interim analysis. [ICH E9]

trial site. Synonym for investigative site, investigator site, site, site of the trial, study site. [ICH E6]

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. See also *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.

trustworthy (electronic records). An attribute of records (data and documents) and signatures submitted to regulatory agencies referring to their suitability for making scientific findings of safety and efficacy that underlie public policy decisions pertaining to market authorization. Two key dimensions that determine the trustworthiness of eClinical trial data are *data quality* and *data integrity*. [after 21CFR Part 11]

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. How treatment arms will be compared (e.g., Safety, Efficacy, PK/PD). May also include comparison to data from other studies or sources (e.g., historical control). [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, whose nature, severity, specificity, or outcome is not consistent with the term or description used in the applicable product information. [ICH E2] See also *adverse drug reaction*.

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

use case. An explicit scenario designed to help in determining whether a system/process is capable of performing the functions required for a particular use. A use case might describe, for example, how a study coordinator would use a tablet computer to capture medical history data.

user site testing (UST). Any testing that takes place outside of the developer's controlled environment. NOTE: Terms such as beta test, site validation, user acceptance test, installation verification, and installation testing have all been used to describe user site testing. User site testing encompasses all of these and any other testing that takes place outside of the developer's controlled environment. [from General Principles of Software Validation; Final Guidance, section 5.2.6]

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. NOTE: Validation is accomplished by planning how to measure and/or evaluate suitability to purpose; then executing the plan and documenting the results. [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 entity 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. Variable is an enveloping term that includes specific subtypes used in clinical research. "Study variable" is a term used in trial design to denote a variable to be captured on the CRF. An "assessment" is a study variable pertaining to the status of a subject. Assessments are usually measured at a certain time, and usually are not compounded significantly by combining several simultaneous measurements to form a derived assessment (e.g., BMI) or a result of statistical analysis. An "endpoint" is a variable that pertains to the trial objectives. Not all endpoints are themselves assessments since certain endpoints might apply to populations or emerge from analysis of results. That is, endpoints might be facts about assessments (e.g., prolongation of survival). When a "variable" is captured or measured, there is no necessary sense that any evaluation or judgment is involved. However, when a variable is to be measured that obviously or actively pertains to subject status, which is always the concern of the physician, that variable becomes or will always be an assessment. The term assessment is intended to invoke some degree of evaluation or judgment concerning subject status. A parameter is most properly a variable pertaining to statistical distributions though the word is often used synonymously with variable by engineers.

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.

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. NOTE: 2. Software verification looks for consistency, completeness, and correctness of the software and its supporting documentation, as it is being developed, and provides support for a subsequent conclusion that software is validated [FDA General Principles of Software Validation; ANSI/ASQC A3-1978; ISO/IEC Guide 25]. Verification is used in the sense of matching elements of a report or results of system testing to individual requirements. *Compare to validation where suitability to purpose is also established.*

verification of data. See *source document verification (SDV)*.

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. [CDISC Trial Design Project]

vocabulary. Terms that function in general reference to concepts that apply over a variety of languages are words, and their totality is a *vocabulary*. *Synonym: terminology*. See *controlled vocabulary*.

volunteer. A person volunteering to participate as a subject in a clinical trial, often a healthy person agreeing to participate in a Phase 1 trial. See *also Phase 1*.

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 a computer monitor.

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

Web server. A computer server that delivers HTML pages or files over the World Wide Web. *See also* 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 subject-initiated act of discontinuing participation in a clinical study. NOTE: Withdrawal can

range from the subject's complete withdrawal from study procedures and follow-up activities, to the subject's withdrawal from study-related interventions while the subject permits continued access to his/her medical records or identifiable information. Note that according to FDA regulations, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. *See also* 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.

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