Clinical Research Glossary

Version 4.0

Orientation: The following Glossary and list of Acronyms, Abbreviations, and Initials is the fourth produced by the Glossary Group 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 Glossary is also to serve the community of clinical researchers by selecting and defining terms pertaining to the conduct of federal- and pharmaceutical industry-sponsored clinical research, particularly eClinical Trials. 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, laboratory methods. The Glossary includes references and links to other glossaries such as regulatory dictionaries or to health-related controlled terminologies that are known to be useful in conducting clinical research.

Glossary terms are organized alphabetically by first word according to the opinion of the Glossary Group 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 term or word is presented first, followed by a period. Terms are defined entities consisting of more than one word. Only proper nouns are capitalized.

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

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

Source(s). The sources for definitions are cited (see "references") 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 definitions, the citation states "after" or "from." Where no source is listed, the definition is from CDISC.

Related words. (optional) These include synonyms ("see") as well as other words ("see also" or "compare to") and comments to sharpen or expand upon the definition.

CDISC Glossary Group

Stephen A. Raymond, Chairperson

Core Committee: **Helle-Mai Gawrylewski,** Johnson and Johnson **Arthur Gertel,** Beardsworth Consulting **Stephen Raymond,** PHT Corporation **Cara Willoughby,** Lilly

Glossary Group Members: **Cathy Barrows,** GSK **Lori J. Brozena,** Merck **Renee Creciun,** Merck **Brenda Duggan,** NCI **Julia Forjanic-Klapproth,** Trilogy Writing **Helle Mai Gawrylewski,** Johnson & Johnson **Arthur Gertel,** Beardsworth Consulting **Kathy Hollinger,** FDA **Rebecca Kush,** CDISC **Elinor Lebner-Olesen,** Novo Nordisk **Jennifer Maginn,** Novo Nordisk **Stephen Raymond,** PHT Corporation **Anne Tompkins,** NCI **Marcella Tordosinsky,** Merck **Karen Underkofler,** SAIC **Cara Willoughby,** Lilly

Glossary Terms

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

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

admission criteria. Basis for selecting target population for a clinical trial. Subjects must be screened to ensure that their characteristics match a list of admission criteria and that none of their characteristics match any single one of the exclusion criteria set up for the study. *See also inclusion criteria, 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 21CFR 310.305 defines an adverse drug experience to include any adverse event, "whether on 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 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 Group] *See also variable.*

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. 1. Documentation that allows reconstruction of the course of events. 2. A secure, time-stamped record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic study record. [1. ICH E6 Glossary; 2. CSUCT]

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 Group]

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.*

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. Prevent identification of treatments/procedures/test to test subjects or study personnel results in order to limit bias (e.g., open-label; single-blind; double-blind). NOTE: Blinding is a procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Includes further distinction between single- and double-blind. Masking, while often used synonymously with blinding, is usually associated with concealing the specific study intervention used. [ICH E9] The term "masking" is often preferred in the field of ophthalmology. [AMA Manual of Style]

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.

certified copy. A copy of original information that has been verified by a certifying signature to preserve accurately the content, information and integrity of the original. The signature can be applied to the copy or be a reference on the copy to a signature on the validation documentation pertaining to an electronic means of accurately copying information.

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

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

clinical protocol. *See protocol.*

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

clinical research associate (CRA). Person employed by a sponsor, or by a contract research organization acting on

a sponsor's behalf, who monitors the progress of investigator sites participating in a clinical study. At some sites (primarily in academic settings), clinical research coordinators are called CRAs.

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

clinical significance. Change in a subject's clinical condition regarded as important whether or not due to the test 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 the ICH Guideline for Structure and Content of Clinical Study Reports. [ICH E6 Glossary]

clinical study. *See clinical trial.*

Clinical trial. Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one of more investigational medicinal product(s), and /or to identify any adverse reactions to one or more investigational medicinal product(s), and/or to study absorption, distribution, metabolism and excretion of one of more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. [Directive 2001/20/EC; Modified from ICH E6 Glossary]

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.

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.*

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]

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 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.*

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 III 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 EMEA'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]

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 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), 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 21CFR 314.126.

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

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

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

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 Group]

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. 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]

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. Contrast with data acquisition, electronic data capture.

data integrity. An attribute of data pertaining to clinical trials depending on the quality of processes for data capture, correction, maintenance, transmission, and retention. Key dimensions of data integrity include that data be attributable, legible, contemporaneous, original and accurate. NOTE: in clinical research the FDA requires that data relied on to determine safety and efficacy of therapies be trustworthy and establishes guidance and regulations concerning practices and system requirements needed to promote an acceptable level of data integrity. [FDA, CSUCT; IEEE]

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 changes.*

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 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 monitoring. Process by which clinical data are examined for completeness, consistency, and accuracy.

data quality. Describes the characteristics that confirm "fitness for use"-that is ability to support meaningful and trustworthy conclusions and interpretations. Quality is established through formal assessment, quality control and auditing. NOTE: Because assessments of data quality are linked to the needs of the study and expectations of the user, the quality criteria may vary from one project to another. *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. Representations of facts, concepts, or instructions in a manner suitable for communication, interpretation, or processing by humans or by automated means. [FDA]

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.

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

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

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

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

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]

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

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: Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subject's identities and sponsor's proprietary information. [ICH E6 Glossary]

discontinuation. The act of concluding participation, prior to completion of all protocol-required elements, in a trial by an enrolled subject NOTE: Four categories of discontinuation are distinguished: a) dropout: Active discontinuation by a subject (also a noun referring to such a discontinued subject); b) investigator-initiated discontinuation (e.g., for cause); c) loss to follow-up: cessation of participation without notice or action by the subject; d) sponsor-initiated discontinuation. 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.*

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.*

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 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 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]

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]

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 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]

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 pharmacopia or formulary. [from FDA Glossary of Terms, CDER]

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 via an audit trail. *See also data entry, data acquisition.*

electronic record. Any combination of text, graphics, data, audio, pictorial, or any other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system. [FDA 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; 21CFR 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 Group, 2. HL7]

eMedical record. An electronic record derived from a computerized system used primarily for delivering patient care in a clinical setting. NOTE: eMedical records may serve as source documents, and such data could serve also as source data for clinical trials provided that the controls on the eMedical record system and the transfer of such data to the eClinical trial system were to fulfill the requirements of 21 CFR Part 11.

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 into a clinical trial; transitive and intransitive. NOTE: Informed consent precedes enrollment, which precedes or is contemporaneous with randomization.

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.

epoch. An interval of time in the planned conduct of a study during which the treatment is consistent. NOTE: Consistent treatment of subjects across arms during an epoch does not mean that the treatment in all arms is the same; rather that the treatment, whatever it is, is to be consistent during the epoch for each arm. *Synonyms: 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 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. 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 data (electronic source data). Source data captured initially into a permanent electronic record used for the reconstruction and evaluation of a trial. 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.*

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

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

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

European Agency for the Evaluation of Medicinal Products (EMEA). 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 trial. Phase I or II trial during which the actions of a therapeutic intervention are assessed and measured. NOTE: Procedures in exploratory trials may appropriately be altered to expand the scope or method of investigation. *Compare to confirmatory trial.*

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 trial.

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

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

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

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

frozen. 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 lock*.

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

gender. Subject self-identification re: Male/ Female. [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]

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

Health Level 7 (HL7). An ANSI-accredited Standards Developing Organization (SDO) operating in the healthcare arena. 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 health care in the ordinary course of business or practice of a profession, including a health care facility. [1. PR Group; 2. HL7]

healthy volunteer. Subject (not a patient) in a clinical trial. NOTE: Usually healthy volunteers serve as subjects in Phase I 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. *Synonyms: independent review board, independent ethics committee, committee for the protection of human subjects.*

intention-to-treat. The principle that asserts that the effect of a treatment policy can be best assessed by evaluating the basis of the intention to treat a subject (i.e., the planned treatment regimen) rather than the actual treatment given. 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 centre). A quantitative interaction refers to the case where the magnitude of the contrast differs at the different levels of the factor; for a qualitative interaction, the direction of the contrast differs for at least one level of the factor.

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

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

Internet. A global system of computer networks that provides the common TCP

IP infrastructure for e-mail, the World Wide Web, and other online activities.

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 trial which has an effect on outcome of interest in a study: e.g., quality of life, efficacy, safety, pharmacoeconomics. *Synonym: therapeutic intervention. 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 trial.

Investigator. 1. 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. 2. The individual "under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team." [1. ICH E6 1.35. 2. From 21CFR 50.3] *See also sponsor-investigator.*

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

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

item. 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.

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 a clinical trial. [2. ODM]

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]

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., 21CFR 201.56 and 201.57 for human prescription drugs, 201.66 for human over-the-counter drugs). *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). The last patient to complete a trial (all data collected), a planned or achieved milestone marked by a date and time. *See also subject, patient, completion.*

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

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

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

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

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

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

marketing support trials. Clinical studies that are designed to improve the sales of a product or to show potential buyers the rationale for 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.

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

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

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

message (HL7). The atomic unit of data transferred between systems. It is comprised of a group of segments in a defined sequence. Each message has a message type that defines its purpose 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. A statistical process for pooling data from multiple clinical trial and summarizing results through formal statistical means.

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)

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

metadata. Data that describe other data

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

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

modem. From modulator/demodulator; a device that converts 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. 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. See also clinical research associate.

monitoring committee. See independent data-monitoring committee.

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

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

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]

multicenter study. See multicenter trial.

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

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

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

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

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

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

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

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

objective. The reason for performing a trial in terms of the scientific questions to be answered by the 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.). *Compare to PRO.* 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 proxy respondent.*

open 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-label study. *See open study*.

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

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

original data. Those values that represent the first recording of study data [CSUCT Definitions]

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] *See also variable; 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 variable or endpoint.*

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

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

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

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

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

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. Often used interchangeably as a synonym for subject but healthy volunteers are not, strictly speaking, patients.*

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

patient reported outcome (PRO). Report coming directly from patients or subjects through interviews or self-completed questionnaires or other data capture tools such as diaries about their life, health condition(s) and treatment. NOTE: PROs are used to assess outcomes involving the patients'/subjects' perceptions, symptoms, satisfaction with treatment, adherence to prescribed regimens. Historically observations on patients have been made by observers, which has produced scientific records lacking high quality data on subjective symptom intensity, perceived benefit, etc. PROs include outcomes recorded by interviewers transcribing the views expressed by the patient, but the term does not apply to outcomes recorded by observers who rely on their own judgment. [DIA ePRO Workgroup, modified by Gordon Guyatt and Holger Schuneman; Patrick, 2003. After Acquardo C., Berzon C., et. al., 2001.] *Synonym: subject reported outcomes (SRO). See also outcome; subject, patient.*

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 apparent or real effect of passing through a period of time designated during the course 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. 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 processes of bodily responses to pharmacological, biochemical, physiological, and therapeutic effects.

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

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

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

pharmacogenomic test. An assay intended to study interindividual

variations in 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 have a good response to a drug, a bad response to a drug, or no response at all.

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

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

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

phase. Clinical trials are generally categorized into four (sometimes five) phases described below. A therapeutic intervention may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases.

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

Phase II. Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. NOTE: Phase II studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects. [FDA]

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

Phase IIIb. A subcategory of Phase III trials done near the time of approval to elicit additional findings. [FDA]

Phase IV. Postmarketing (Phase IV) 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 II studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time. [FDA]

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

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

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

postmarketing surveillance. Ongoing safety monitoring of marketed drugs. *See also Phase IV studies, Phase V studies.*

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

preclinical studies. Animal studies that support Phase I safety and tolerance studies and must comply with good laboratory practice (GLP). Data about a drug's activities and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical studies or trials).

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 Group; 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]

proprietary name. A commercial name granted by a naming authority for use in marketing a drug/device product. [SPL] *Synonym: 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. [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 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 Group; 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.*

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. Proxy outcomes seem to be part of the outcomes literature with a consistent meaning. [CDISC (extension of SDTM based on Table 2 Patrick, DL, 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 DL, 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.

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").

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]

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, 2003] *Compare to psychometric validation; see also validation.*

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.*

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 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]

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.

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

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.

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.

secondary objective. *See objective.*

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

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

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; 21CFR11.10(a); ISO 9000-3; Huber, L. (1999) *See also validation, verification. Verification also 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.

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

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

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 document verification. The process by which the information reported by an investigator is compared with the original records to ensure that it is complete, accurate and valid. [Schuyl 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 medico-technical departments involved in the clinical trial). [ICH; CSUCT]

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, management, and/or financing of a clinical trial. 2. A corporation or agency whose employees conduct the investigation is considered a sponsor and the employees are considered investigators. [1. ICH. 2. 21 CFR 50.3]

sponsor-investigator. An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. 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 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 the FDA or other health authority, considered to be effective in the treatment of a specific disease or condition .

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

statistical 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.

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

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

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

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

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. Diagrammatic representation of key activities within the study.

study population. Defined by protocol inclusion/exclusion criteria.

study protocol. *See protocol.*

study variable. A term used in trial design to denote a variable to be captured on the CRF. *See 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 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, 2003] *See also patient reported outcome (PRO).*

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]

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]

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

technology provider. A person, company or other entity who develops, produces and sells software applications and/or hardware for use in conducting clinical trials and/or in analyzing clinical trial data and or submitting clinical trial information for regulatory approval. *Synonym: vendor.*

term. Single glossary entry composed of more than one word.

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

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

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

therapeutic intervention. *See intervention.*

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.

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

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

trial subject. Subject in a clinical trial. *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.

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. [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. actmagazine.com, for example.

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

validation. 1. Process of establishing suitability to purpose. 2. For software and systems, establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes. 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, psychometric. *See psychometric validation.*

validity. *See validation.*

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

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

Reference Citations

- 21 CFR 820.20. Available at http://www.fda.gov (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=820.20)
- 21 CFR Part 11. Electronic Records; Electronic Signatures Final Rule, 62 Federal Register 13430 (March 20, 1997). Available at http://www.fda.gov (*Code of Federal Regulations*)
- A Drug Review Glossary. Available at: http://www.fda.gov/fdac/special/newdrug/bengloss.html
- C. Acquardo, C. Berzon *et al.* Incorporating the Patient's Perspective into Drug Development and Communication: An Ad Hoc Task force Report of the Patient-Reported Outcomes (PRO) Harmonization Group Meeting at the Food and Drug Administration, Feb. 16, 2001, *Value in Health,* 6 (5) 522–531 (2001).
- D.G. Altman, K.F. Schultz, D. Moher *et al.,* "The Revised CONSORT Statement for Reporting Randomized Trials: Explanation and Elaboration," *Ann Intern Med.*, 134, 663–694 (2001). Available at: http://www.consort-statement.org/
- *American Medical Association Manual of Style, a guide for authors and editors. 9th Ed.* (Baltimore, MD: Williams & Wilkins, 1998).
- Analysis Dataset Model (CDISC). Available at http://www.cdisc.org/standards/index.html
- Biomarkers Definitions Working Group: Biomarkers and Surrogate Endpoints: Preferred Definitions and Conceptual Framework. *Clin Pharmacol Ther*, 69, 89–95 (2001).
- *Center for the Advancement of Clinical Research – Clinical Research Dictionary*. Available at: http://www.med.umich.edu/cacr/dictionary/A-B/htm
- Document type definition from: http://www.XMLfiles.com
- Federal Information Processing Standards (FIPS) Publication 46-2. 1993 December 30. Available at: http://www.itl.nist.gov/fipspubs/fip46-2.htm
- General Principles of Software Validation; Final Guidance for Industry and FDA Staff, Jan 11, 2002. Available at http://www.fda.gov/cdrh/comp/guidance/938.pdf or www.fda.gov/cber/guidelines.htm
- W. Ed Hammond, Glossary for Healthcare Standards, 1995. Available at http://dmi-www.mc.duke.edu/dukemi/acronyms.htm
- Glossary of Computerized System and Software Development Terminology, Division of Field Investigations, Office of Regional Operations, Office of Regulatory Affairs, Food and Drug Administration, August 1995. Available at: http://www.fda.gov/ora/inspect_ref/igs/gloss.html
- Guidance for industry: Computerized Systems Used in Clinical Trials. CSUCT definitions, 1999. http://www.fda.gov/ora/compliance_ref/bimo/ffinalcct.htm New Draft available at: http://www.fda.gov/cder/guidance/6032dft.htm
- G.H. Guyatt, D.H. Feeney, D.L. Patrick, "Measuring Health-Related Quality of Life," *Ann Internal Medicine*, 118, 622–629 (1993).
- HL7 Glossary of Terms. January 2002. Available at: https://www.hl7.org/library/bookstore/
- L. Huber, "In Search of Standard Definitions for Validation, Qualification, Verification and Calibration," *BioPharm,* 12 (4) 56–58 (1999).
- HyperStat Online Glossary. Available at: http://davidmlane.com/hyperstat/glossary.html
- ICH Efficacy Guideline page (E2a, E3, E6, E7, E8, E9, E10, E11). Available at: http://www.ich.org/cache/compo/276-254-1.html
- *IEEE Standard Computer Dictionary*; a compilation of IEEE standard computer glossaries, 1990.
- ISO 9000-3:1997, Quality management and quality assurance standards – Part 3: Guidelines for the application of ISO 9001:1994 to the development, supply, installation and maintenance of computer software. International Organization for Standardization, 1997.
- ISO/IEC/IEEE 12207:1995 §3.35; from ISO/IEC 12207:1995, Information technology – Software life cycle processes, Joint Technical Committee ISO/IEC JTC 1, Subcommittee SC 7, International Organization for Standardization and International Electrotechnical Commission, 1995.
- R. Khosla, D.D. Verma, A. Kapur *et al.*," Efficient Source Data Verification," *Indian J. Pharm,* 32, 180–186 (2000).
- D.L. Patrick, "Patient-Reported Outcomes (PROs): An Organizing Tool for Concepts, Measures, and Applications," *MAPI Quality of Life News Letter,* 31, 1–5 (2003).
- Protocol Representation Group (PR Group), CDISC, Protocol Elements Spreadsheet, 2005. Available at: http://www.cdisc.org/standards/index.html
- M.L. Schuyl and T. Engel, "A Review of the Source Document Verification Process in Clinical Trials," *DIA Journal* ,33, 789–797 (1999).
- Structured Product Labeling (SPL). Available at : https://www.hl7.org.library/bookstore/
- Study Data Tabulation Model (SDTM). Available at http://www.cdisc.org/standards/index.html
- The WHO Group, "The Development of the World Health Organization Quality of Life Assessment Instrument (WHOQOL)," in J. Orley and W. Kuyken (Eds.), *Quality of Life Assessment: International Perspectives* (Berlin, Heidelberg: Springer-Verlag, p. 41, 1994).

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

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

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

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

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