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Standard Terminology Relating to Process Analytical Technology in the Pharmaceutical Industry[1]

This standard is issued under the fixed designation E2363; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This terminology covers process analytical technology in the pharmaceutical industry. Terms are defined as they are used relative to the PAT framework in the pharmaceutical industry. Terms that are generally understood and in common usage or adequately defined in other readily available eferences are not included except where particular delineation to process analytical technology may be more clearly stated.

1.2 This terminology is therefore intended to be selective of terms used generally in process analytical technology as it is applied in the pharmaceutical industry and published in a number of documents, such as those listed in the succeeding sections. The listing is also intended to define terms that appear prominently within other related ASTM standards and do not appear elsewhere.

1.3 The definitions are substantially identical to those published by the U.S. Food and Drug Administration and other authoritative bodies, such as ISO, IEC, ITU, and national standards organizations.

1.4 This terminology supplements current documents on terminology that concentrate on process analytical technology as it is applied in the pharmaceutical industry.

1.5 An increasing number of product designations and designations for chemical, physical, mechanical, analytical, and statistical tests and standards are coming into common usage in the literature, regulatory environment, and commerce associated with process analytical technology in the pharmaceutical industry. Section 2 lists those documents referenced in this terminology.

1.6 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E456 Terminology Relating to Quality and Statistics

E869 Test Method for Performance Evaluation of Fuel Ethanol Manufacturing Facilities

E1117 Practice for Design of Fuel-Alcohol Manufacturing Facilities

E1126 Terminology Relating to Biomass Fuels (Withdrawn 2003)[3]

E1285 Guide for Identification of Bacteriophage Lambda (λ) or Its DNA (Withdrawn 2014)[3]

E1286 Guide for Identification of Herpes Simplex Virus or Its DNA (Withdrawn 2014)[3]

E1287 Practice for Aseptic Sampling of Biological Materials (Withdrawn 2008)[3]

E1298 Guide for Determination of Purity, Impurities, and Contaminants in Biological Drug Products (Withdrawn 2014)[3]

E1342 Practice for Preservation by Freezing, Freeze-Drying, and Low Temperature Maintenance of Bacteria, Fungi, Protista, Viruses, Genetic Elements, and Animal and Plant Tissues (Withdrawn 2011)[3]

E1344 Guide for Evaluation of Fuel Ethanol Manufacturing Facilities

E1493 Guide for Identification of Bacteriophage M13 or Its DNA (Withdrawn 2014)[3]

E1531 Practice for Detection of Mycoplasma Contamination of Cell Cultures by Growth on Agarose Medium (Withdrawn 2014)[3]

E1532 Practice for Detection of Mycoplasma Contamination of Cell Cultures by Use of Bisbenzamide DNA-Binding Fluorochrome (Withdrawn 2014)[3]

E1533 Practice for Indirect Detection of Mycoplasma in Cell Culture by 4'-6-Diamidino-2-2 Phenylindole (DAPI) Staining (Withdrawn 2014)[3]

[1] This terminology is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.91 on Terminology.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] The last approved version of this historical standard is referenced on www.astm.org.

E1536 Practice for Detection of Mycoplasma Contamination of Bovine Serum by Large Volume Method (Withdrawn 2014)[3]
E1564 Guide for Design and Maintenance of Low-Temperature Storage Facilities for Maintaining Cryopreserved Biological Materials
E1565 Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures
E1566 Guide for Handling Hazardous Biological Materials in Liquid Nitrogen
E2500 Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment
E2629 Guide for Verification of Process Analytical Technology (PAT) Enabled Control Systems

2.2 *U.S. Government Publications:*[4]
21 CFR 210.3(b) Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General—Definitions
21 CFR 314.3(b) Applications for FDA Approval to Market a New Drug—General Provisions—Definitions

2.3 *ICH Publications:*[5]
ICH R2 (Q1) Validation of Analytical Procedures: Text and Methodology
ICH Q6A Guidance for Industry—Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances
ICH Q6B Guidance for Industry—Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
ICH Q7 Guidance for Industry—Good Manufacturing Practice Guide For Active Pharmaceutical Ingredients
ICH Q8 (R2) Guidance for Industry—Pharmaceutical Development
ICH Q9 Guidance for Industry—Quality Risk Management
ICH Q10 Guidance for Industry—Pharmaceutical Quality System
ICH Q11 Guidance for Industry—Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities)

2.4 *ISO Publications:*[6]
ISO 9000:2005 Quality Management Systems—Fundamentals and Vocabulary
ISO EN 14971:2012 Medical Devices—Application of Risk Management for Medical Devices
ISO/IEC Guide 51:2014 Safety Aspects—Guidelines for Their Inclusion in Standards
ISO Guide 73:2009 Risk Management—Vocabulary

2.5 *Other Publication:*
EU GMP Glossary

[4] Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401, http://www.access.gpo.gov.

[5] Available from International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), ICH Secretariat, c/o IFPMA, 15 ch. Louis-Dunant, P.O. Box 195, 1211 Geneva 20, Switzerland, http://www.ich.org.

[6] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

3. Terminology

3.1 *Definitions:*

acceptance criteria, *n*—numerical limits, ranges, or other suitable measures for acceptance of test results. **ICH Q7**

accuracy, *n*—the accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. **ICH Q8 (R2)**

active pharmaceutical ingredient (API) (or drug substance), *n*—any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body. **ICH Q7**

analytical procedure, *n*—the analytical procedure refers to the way of performing the analysis. It should describe in detail the steps necessary to perform each analytical test. This may include but is not limited to: the sample, the reference standard and the reagents preparations, use of the apparatus, generation of the calibration curve, use of the formulae for the calculation, etc. **ICH Q8 (R2)**

analyzer, *n*—an instrument designed to measure and report a property of the process, material, or environmental condition.

API starting material, *n*—a raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API Starting Materials are normally of defined chemical properties and structure. **ICH Q7**

at-line measurements, *n*—measurement where the sample is removed, isolated from, and analyzed in close proximity to the process stream.

attribute, *n*—a characteristic or inherent property or feature.

batch, *n*—a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture. **21 CFR 210.3(b)**

batch number, *n*—See **lot number**.

batch process, *n*—a noncontinuous operation in which discrete quantities of material are transformed using individual or sequential steps. **21 CFR 210.3(b)**

bioburden, *n*—the level and type (for example, objectionable or not) of micro-organisms that can be present in raw materials, API starting materials, intermediates or APIs. Bioburden should not be considered contamination unless

the levels have been exceeded or defined objectionable organisms have been detected. **ICH Q7**

calibration, *n*—the demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements. **ICH Q7**

capability of a process, *n*—ability of a process to realize a product that will fulfil the requirements of that product. The concept of process capability can also be defined in statistical terms. **ISO 9000:2005, ICH Q10**

change management, *n*—a systematic approach to proposing, evaluating, approving, implementing, and reviewing changes. **ICH Q10**

chemical transformation step, *n*—for chemical entities, a step involved in the synthesis of the chemical structure of the drug substance from precursor molecular fragments. Typically it involves C-X or C-C bond formation or breaking. **ICH Q11**

computer system, *n*—a group of hardware components and associated software designed and assembled to perform a specific function or group of functions. **ICH Q7**

computerized system, *n*—a process or operation integrated with a computer system. **ICH Q7**

contaminants, *n*—any adventitiously introduced materials (for example, chemical, biochemical, or microbial species) not intended to be part of the manufacturing process of the drug substance or drug product. **ICH Q6B**

contamination, *n*—the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, API (active pharmaceutical ingredient), or dosage form during production, sampling, packaging, or repackaging, storage, or transport. **ICH Q7**

continual improvement, *n*—recurring activity to increase the ability to fulfil requirements. **ISO 9000:2005**

continuous process—a process in which material is added, processed, and removed in an uninterrupted manner.

continuous process verification, *n*—an alternative approach to process validation in which manufacturing process performance is continuously monitored and evaluated. **ICH Q8 (R2)**

contract manufacturer, *n*—a manufacturer who performs some aspect of manufacturing on behalf of another entity.

control number, *n*—See **lot number**.

control model, *n*—procedure or mathematical expression (algorithm) that uses the outputs of the process model combined with any other data inputs required to calculate values for the critical control parameters for the process; it uses input data from the process to generate an actionable command or commands that are issued to the control system. **E2629**

control strategy, *n*—a planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. **ICH Q10**

control system, *n*—system that responds to inputs signals from the process, its associated equipment, other programmable systems, or an operator, or combinations thereof, and generates output signals causing the process and its associated equipment to operate in the desired manner. **E2629**

corrective action, *n*—action to eliminate the cause of a detected non-conformity or other undesirable situation. **ISO 9000:2005**

DISCUSSION—Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.

critical, *n*—describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification. **ICH Q7**

cross-contamination, *n*—contamination of a material or product with another material or product. **ICH Q7**

current good manufacturing practices (CGMP), *n*—current regulations published by the United States Food and Drug Administration (FDA) regarding manufacturing, processing, packaging and storing of drug and biological products. **E1287**

decision maker(s), *n*—person(s) with the competence and authority to make appropriate and timely quality risk management decisions. **ICH Q9**

detectability, *n*—the ability to discover or determine the existence, presence, or fact of a hazard. **ICH Q9**

detection limit, *n*—the detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. **ICH R2 (Q1)**

Design of Experiments (DoE), *n*—the arrangement in which an experimental program is to be conducted, and the selection of the levels (versions) of one or more factors or factor combinations to be included in the experiment. **E456**

design reviews, *n*—planned and systematic reviews of specifications, design, and design development and continuous improvement changes performed as appropriate throughout the life-cycle of the manufacturing system. Design reviews evaluate deliverables against standards and requirements, identify problems, and propose required corrective actions. **E2500**