



Standard Terminology Relating to Process Analytical Technology in the Pharmaceutical Industry¹

This standard is issued under the fixed designation E 2363; 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 reappraisal. A superscript epsilon (ε) indicates an editorial change since the last revision or reappraisal.

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 references 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.

2. Referenced Documents

2.1 U.S. Government Publications:

- 21 CFR 314.3(b) Applications for FDA Approval to Market a New Drug—General Provisions—Definitions²
U.S. FDA PAT Guidance Document, Guidance for Industry

¹ This terminology is under the jurisdiction of ASTM Committee E55 on Pharmaceutical Application of Process Analytical Technology and is the direct responsibility of Subcommittee E55.91 on Terminology.

Current edition approved Jan. 15, 2006. Published January 2006. Originally approved in 2004. Last previous edition approved in 2005 as E 2363 – 05b.

² Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401.

PAT—A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance³
FDA/ICH Q7A Guidance Document, GMP Guidance for APIs and Its Use During Inspections³

2.2 Other Publication:

ISO EN 14971 Medical Devices—Application of Risk Management for Medical Devices⁴

3. Terminology

3.1 Definitions:

acceptance criteria, *n*—numerical limits, ranges, process signatures, or other suitable measures that are necessary for making a decision to accept or reject the result of a process, in-process variable, a product or any other convenient subgroups of manufactured units.

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

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

batch number, *n*—a combination of numbers, letters, and/or symbols that uniquely identifies a batch and from which the production and distribution history can be determined.

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

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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.

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

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

³ Available from Food and Drug Administration, 5600 Fishers Ln., Rockville, MD 20857.

⁴ Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036.

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deviation, *n*—departure from an approved instruction or established standard.

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drug product, *n*—a drug product is a finished dosage form (for example, tablets, capsule, or solution) that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

21 CFR 314.3(b)

impurity, *n*—any component present in a raw material, intermediate, API, or dosage form that is not the desired entity.

impurity profile, *n*—a description of the identified and unidentified impurities present in a raw material, intermediate, API, or dosage form.

in-line measurements, *n*—measurement where the sample is not removed from the process stream, and can be invasive or non-invasive.

in-process material, *n*—any material(s) fabricated, compounded, blended, or synthesized using a chemical, physical, or biological process that is produced for and being used in the preparation of an intermediate, drug substance, or drug product.

in-process tests, *n*—measurements performed during manufacturing and pertaining to the process or products within the process.

intermediate, *n*—material produced during manufacture that undergoes further change or purification. Intermediates may or may not be isolated.

lot number, *n*—see **batch number**.

manufacture, *n*—all operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage, and distribution of APIs or drug products and related controls.

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manufacturing process, *n*—a set of activities or operations performed to deliver a desired output.

material, *n*—a general term used to denote raw materials (starting materials, reagents, solvents), process aids, intermediates, APIs, and packaging and labeling materials.

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mother liquor, *n*—the residual liquid that remains after the crystallization or isolation processes.

DISCUSSION—A mother liquor may contain unreacted materials, intermediates, API, and/or impurities. It can be used for further processing.

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off-line measurements, *n*—measurement where the sample is removed, isolated from, and analyzed in an area remote from the manufacturing process.

on-line measurements, *n*—measurement where the sample is diverted from the manufacturing process, and may be returned to the process stream.

packaging material, *n*—any material intended to contain and protect a raw material, intermediate, API, or product during storage and transport.

parametric release, *n*—a system of release that gives assurance that the product is of the intended quality based on the information collected during the manufacturing process.

procedure, *n*—a documented description of the operations to be performed, the precautions to be taken, and the measures

to be applied directly or indirectly related to the manufacture of an intermediate, API, or drug product.

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process aids, *n*—materials, excluding solvents, used as an aid in the manufacture of an intermediate or API that do not themselves participate in a chemical or biological reaction (for example, filter aid, activated carbon).

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process analytical technology (PAT), *n*—system for designing, analyzing, and controlling manufacturing through timely measurements of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.

U.S. FDA PAT Guidance

process control, *n*—checks performed during manufacturing to measure critical attributes and, if appropriate, adjust the process to deliver the desired output(s).

FDA/ICH Q7A Guidance

process parameter, *n*—an attribute of the manufacturing system.

qualification, *n*—action of proving and documenting that those aspects of equipment or systems that affect product or process quality, or both, are properly designed, fabricated, installed, work, and perform as specified.

quality assurance (QA), *n*—the sum total of the organized arrangements made with the object of ensuring that all APIs or drug products are of the quality required for their intended use and that quality systems are maintained.

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quality unit(s), *n*—an organizational unit independent of production that fulfills both quality assurance and quality control responsibilities.

DISCUSSION—This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.

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quarantine, *n*—the status of materials isolated physically or by other effective means pending a decision on their subsequent approval or rejection.

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raw material, *n*—a general term used to denote starting materials, reagents, and solvents intended for use in the production of intermediates, APIs, or products.

reference standard, primary, *n*—a substance that has been shown by an extensive set of analytical tests to be authentic material that should be of high purity.

DISCUSSION—This standard can be: (1) obtained from an officially recognized source, (2) prepared by independent synthesis, (3) obtained from existing production material of high purity, or (4) prepared by further purification of existing production material.

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reference standard, secondary, *n*—a substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis.

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retest date, *n*—the date when a material should be re-examined to ensure that it is still suitable for use.

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risk, *n*—combination of the probability of occurrence of harm and the severity of that harm. **ISO EN 14971**

risk analysis, *n*—systematic use of available information to identify hazards and to estimate risk. **ISO EN 14971**

risk assessment, *n*—overall process comprising a risk analysis and a risk evaluation. **ISO EN 14971**

safety, *n*—freedom from unacceptable risk. **ISO EN 14971**

sample, *n*—a portion, piece, or segment that is representative of a whole.

solvent, *n*—an inorganic or organic liquid used as a vehicle for the preparation of solutions or suspensions in the manufacture of an intermediate, API, or drug product.

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starting material, *n*—a raw material, intermediate, or an API that is used in the production of an API or product and that is incorporated as a significant structural fragment into the structure of the API or dosage form.

DISCUSSION—A 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. Starting materials are normally of defined chemical properties and structure.

validation protocol, *n*—a written plan stating how validation will be conducted and defining acceptance criteria.

DISCUSSION—For example, the protocol for a manufacturing process identifies processing equipment, critical process parameters and/or operating ranges, product characteristics, sampling, test data to be collected, number of validation runs, and acceptable test results.

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yield, expected, *n*—the quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot scale, or manufacturing data.

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yield, theoretical, *n*—the quantity that would be produced at any appropriate phase of production based upon the quantity of material to be used, in the absence of any loss or error in actual production.

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