Designation: E2810 – 23

Standard Practice for Demonstrating Capability to Comply with the Test for Uniformity of Dosage Units[1]

This standard is issued under the fixed designation E2810; 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 practice provides a general procedure for evaluating the capability to comply with the Uniformity of Dosage Units (UDU) test. This test is given in General Chapter <905> Uniformity of Dosage Units of the USP, in 2.9.40 Uniformity of Dosage Units of the Ph. Eur., and in 6.02 Uniformity of Dosage Units of the JP, and these versions are virtually interchangeable. For this multiple-stage test, the procedure computes a lower bound on the probability of passing the UDU test, based on statistical estimates made at a prescribed confidence level from a sample of dosage units.

1.2 This methodology can be used to generate an acceptance limit table, which defines a set of sample means and standard deviations that assures passing the UDU test for a prescribed lower probability bound, confidence level, and sample size.

1.3 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.4 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E2363 Terminology Relating to Manufacturing of Pharmaceutical and Biopharmaceutical Products in the Pharmaceutical and Biopharmaceutical Industry

E2709 Practice for Demonstrating Capability to Comply with an Acceptance Procedure

2.2 *Other Documents:*

JP Japanese Pharmacopoeia[3]

Ph. Eur. European Pharmacopoeia[4]

USP United States Pharmacopeia[5]

3. Terminology

3.1 *Definitions*—See Terminology E2363 for a more extensive listing of terms in ASTM Committee E55 standards.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *acceptable parameter region, n*—the set of values of parameters characterizing the distribution of test results for which the probability of passing the lot acceptance procedure is greater than a prescribed lower bound.

3.2.2 *acceptance limit, n*—the boundary of the acceptance region, for example, the maximum sample standard deviation for a given sample mean or minimum and maximum sample mean for given standard deviations.

3.2.2.1 *Discussion*—The coefficient of variation (relative standard deviation) may be substituted for the standard deviation where applicable.

3.2.3 *acceptance region, n*—the set of values of parameter estimates (that is, sample mean and standard deviation) where confidence limits attain a prescribed lower bound on the probability of passing a lot acceptance procedure.

3.2.4 *confidence level, C, n*—the prescribed overall level for calculating the uncertainty region of the parameters from the sample estimates.

3.2.4.1 *Discussion*—The preset confidence level is stated as a percentage, for example, $100\,(1-\alpha) = 95\,\%$, where α is a risk that is allocated to the two parameters being estimated.

[1] This practice is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.14 on Measurement Systems and Analysis.

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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] Available from the Pharmaceuticals and Medical Devices Agency (PMDA), Shin-Kasumigaseki Building, 3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013, Japan, https://www.pmda.go.jp.

[4] Available from the European Directorate for the Quality of Medicines and Health Care (EDQM), Council of Europe, 7 allée Kastner, CS 30026, F-67081 Strasbourg, France, http://www.edqm.eu.

[5] Available from U.S. Pharmacopeial Convention (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

3.2.5 *lower probability bound, LB, n*—the nominal probability of passing the UDU test for a given set of parameter estimates.

3.2.6 *multiple-stage acceptance procedure, n*—a procedure that involves more than one stage of sampling and testing a given quality characteristic with one or more acceptance criteria per stage.

3.2.7 *representative sample, n*—a sample that consists of a number of units that are drawn based on rational criteria such as random, stratified, or systematic sampling and intended to assure that the sample accurately portrays the material being sampled.

3.2.8 *sampling plan, n*—scheme for selecting dosage units from locations within a batch for testing purposes.

3.2.8.1 *Discussion*—In this standard, either a single dosage unit is selected from each batch location (called Sampling Plan 1) or an equal but greater than one dosage unit is selected from each batch location (called Sampling Plan 2).

3.2.9 *uniformity of dosage units, UDU, n*—the degree of uniformity in the amount of the drug substance among dosage units.

3.2.9.1 *Discussion*—The requirements of the UDU test apply to each drug substance in dosage units containing one or more drug substances, unless otherwise specified. The uniformity improves as the variability decreases.

4. Significance and Use

4.1 The methodology was originally developed **(1-4)**[6] for use in drug content uniformity and dissolution but has general application to any multistage test with multiple acceptance criteria. Practice E2709 summarizes the statistical aspects of this methodology. This practice applies the general methodology of Practice E2709 specifically to the UDU test.

4.1.1 While other methods can be used to estimate the probability of passing the UDU test, they are outside the scope of this practice.

4.2 The UDU test procedure describes a two-stage sampling test, where at each stage one can pass or continue testing, and the decision to fail is deferred until the second stage. At each stage there are acceptance criteria on the test results as outlined in Table 1.

4.3 The UDU test is a market standard. The USP General Notices include the following statement about compendial standards. “The similarity to statistical procedures may seem to suggest an intent to make inference to some larger group of units, but in all cases, statements about whether the compendial standard is met apply only to the units tested.” Therefore, the

[6] The boldface numbers in parentheses refer to a list of references at the end of this standard.

TABLE 1 Uniformity of Dosage Units Test Procedure

NOTE 1—All measurements of dosage units and criteria values are in percentage label claim (%LC). At each stage calculate the sample average, $\bar{X}$, and the sample standard deviation, s.

Stage	Number Tested	Pass Stage If:
S_1	10	$\lvert M - \bar{X}\rvert + 2.4\ s \le 15.0$, where M is defined below.
S_2	20	(*1*) $\lvert M - \bar{X}\rvert + 2.0\ s \le 15.0$, using all 30 results ($S_1 + S_2$). (*2*) No dosage unit is outside the maximum allowed range of 0.75 * M to 1.25 * M.

M is defined as follows:

If T is less than or equal to 101.5 %LC, and
(*1*) If $\bar{X}$ is less than 98.5 %LC, then M = 98.5 %LC.
(*2*) If $\bar{X}$ is between 98.5 and 101.5 %LC, then $M = \bar{X}$.
(*3*) If $\bar{X}$ is greater than 101.5 %LC, then M = 101.5 %LC.

If T is greater than 101.5 %LC, and
(*1*) If $\bar{X}$ is less than 98.5 %LC, then M = 98.5 %LC.
(*2*) If $\bar{X}$ is between 98.5 and T, then $M = \bar{X}$.
(*3*) If $\bar{X}$ is greater than T, then $M = T$.

T is the target content per dosage unit at the time of manufacture, expressed as %LC. Unless otherwise specified in the individual monograph, T is 100.0 %LC.