Revision proposals published in *Pharmacopeial Forum* often elicit public comments that are forwarded to the appropriate Expert Committee for review and response. In accordance with the Rules and Procedures of the 2005-2010 Council of Experts, revision proposals can advance to official status with minor modifications, as needed, without requiring further public review. In such cases a summary of comments received and the appropriate Expert Committee's responses are published in the *Commentary* section of the USP website at the time the revision becomes official. For those proposals that require further revision and republication in *Pharmacopeial Forum*, a summary of the comments and the Expert Committee's responses will be included in the briefing that accompanies each article.

The *Commentary* section is not part of the official text of the monograph and is not intended to be enforceable by regulatory authorities. Rather, it explains the basis of the Expert Committee's response to public comments. If there is a difference between the contents of the *Commentary* section and the official monograph, the text of the official monograph prevails. In case of a dispute or question of interpretation, the language of the official text, alone and independent of the *Commentary* section, shall prevail.

For further information, contact:
The USP Executive Secretariat
U.S. Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA
execsec@usp.org

USP Monographs

Monograph/Section(s): Baclofen/Assay
Expert Committee(s): MD-PP
No. of Commenters: 1
Comment Summary: The comment requested the sample size be increased from 40 mg to 200 mg to increase the accuracy of endpoint detection.
Response: Comment incorporated.

Monograph/Section(s): Biological Indicators for Moist Heat, Dry Heat, and Gaseous Modes of Sterilization, Liquid Spore Suspensions/Multiple Sections
Expert Committee(s): MSA
No. of Commenters: 3
Comment Summary #1: One comment suggested revising the low end of the labeled spore count from 10^4 to 10^3 in the Definition section because most common sterilization processes are robust and because at low concentrations, indicators with spore populations as low as 5×10^3 would be appropriate and preferred.
Response: Comment incorporated.

Comment Summary #2: One comment suggested that the Kill time statement be changed to add a 1:100 dilution statement. This change would keep the Kill time statement in alignment with the Survival time statement.
Response: Comment incorporated.
Expert Committee-initiated change: The Committee revised to the Identification section to remove the ID test for specific organisms because identification of the biological indicator is of lesser importance than population and resistance to the sterilization process. The section now indicates that the manufacturer should identify in the labeling the species utilized. In addition, the Expert Committee revised the D-value to align it with the D-values of related monographs including Biological Indicators for Moist Heat, Dry Heat, and Gaseous Modes of Sterilization, Non-Paper Carriers.

Monograph/Section(s): Biological Indicators for Moist Heat, Dry Heat, and Gaseous Modes of sterilization, Non-Paper Carriers/Multiple Sections
Expert Committee(s): MSA
No. of Commenters: 3
Comment Summary #1: There were 3 suggestions for modifying the monograph Definition. The commenters suggested using the term “other than paper strip” to accommodate the various types of available spore carriers and emphasizing that cultures other than those specified may be used for inoculating metal and plastic carriers. They also suggested changing the low end of the labeled spore count from 10^4 to 10^3 because most common sterilization processes are robust and because at low concentrations, indicators with spore populations as low as 5×10^3 would be appropriate and preferred.
Response: Comments incorporated.
Comment Summary #2: It was suggested that the Expiration date section be modified to state "The expiration date is determined on the basis of stability studies and is not more than 18 months from the date of manufacture." The expiration date on most biological indicators is 12 months or less.
Response: Comments incorporated.
Comment Summary #3: A number of suggestions were received regarding the monograph Labeling section. It was suggested to replace the term “metal carrier” with “specific substrate” to clarify that non-metal carriers may be acceptable. A commenter suggested clarifying that the expiration date may appear on the package insert or labeling instead of the label. Another commenter suggested deleting the requirement to include the size of the carrier in the labeling, because other more important parameters are addressed in labeling.
Response: Comments incorporated.
Comment Summary #4: In the D-value test, it was suggested to change “sterilizing temperature” to “sterilizing conditions” to assure the monograph is applicable to current gaseous sterilization technologies.
Response: Comment incorporated.
Expert Committee-initiated change: The committee revised the Identification section to indicate that the manufacturer of the biological indicator should identify the organism used. The committee also revised the D-Value section to indicate that the manufacture should specify the method used to determine the labeled D-value.

Monograph/Section(s): Calcium Carbonate and Magnesia Chewable Tablets/Labeling
Expert Committee(s): MD-GRE and NOM
No. of Commenters: 1
Comment Summary: The comment was to revise the labeling section to be consistent with the definition for Chewable Tablets.
Response: Comment incorporated (also see *Calcium Carbonate and Magnesia Tablets*).

Monograph/Section(s): Calcium Carbonate and Magnesia Tablets/Labeling
Expert Committee(s): MD-GRE and NOM
No. of Commenters: 0
Expert Committee-initiated change: Based on the comment received for Calcium Carbonate and Magnesia Chewable Tablets, the Nomenclature Expert Committee initiated a revision to the labeling section of this monograph so it is consistent with the definition for Chewable Tablets.

Monograph/Section(s): Citalopram Hydrobromide/pH
Expert Committee(s): MD-PP
No. of Commenters: 1
Comment Summary: The commenter requested the pH range be widened.
Response: Comment not incorporated because inadequate supporting data were provided.

Monograph/section(s): Estradiol Benzoate/new monograph/multiple sections
Expert Committee(s): VET05
No. of Commenters: 2
Comment Summary #1: The commenters suggested revising the Residue on ignition test to specify that the quantity of material needed for testing is 250 mg and the acceptance criteria should be 0.2%
Response: Comment incorporated.
Comment Summary #2: A commenter suggested revising the Particle size test by changing the vortex time from “10 minutes” to “1 minute.”
Response: Comment incorporated.
Comment Summary #3: A commenter suggested revising the Limit of methanol and dichloromethane test by adding a note requiring the pyridine used in preparing the Internal standard solution is suitably qualified.
Response: Comment incorporated.
Comment Summary #4: One commenter suggested changing the Labeling statement to indicate that “fine grade” material is material that complies with the Particle size test.
Response: Comment not incorporated, as the grade of the article is considered an important attribute.
Comment Summary #5: It was suggested to replace the monograph tests for Chromatographic purity and HPLC Assay with the European Pharmacopoeia monograph tests for Related substances and titrimetric Assay, respectively.

Response: Comment not incorporated. The Committee indicates a preference for an HPLC-based Assay over a titrimetric procedure. The Committee will consider an alternate HPLC procedure and revised procedures for chromatographic purity upon receipt of supporting data.

Monograph/Section(s): Esomeprazole Magnesium/Multiple Sections
Expert Committee(s): MD-GRE
No. of Commenters: 8
Comment Summary #1: Minor changes in the Identification-B test were requested.
Response: Comment incorporated.
Comment Summary #2: A commenter requested deletion of the capacity factor from the monograph system suitability requirements.
Response: Comment incorporated because the capacity factor is not critical to chromatographic separation.
Comment Summary #3: Two commenters requested that other hydrated and amorphous API forms be included in the monograph and different Specific Rotation limits be established for them.
Response: Comment not incorporated. The Expert Committee is willing to consider future changes to this monograph upon receipt of supporting information.
Comment Summary #4: One commenter requested the Enantiomeric purity test be deleted and the Specific rotation test be used to monitor for the stereochemical identity and purity of active ingredient while another commenter requested the Specific rotation test be deleted and the Enantiomeric purity test be used to monitor for the stereochemical identity and purity of active ingredient.
Response: Comments not incorporated. The Expert Committee is willing to consider future changes to this monograph upon receipt of supporting data.

Monograph/Section(s): Fludarabine Phosphate Injection/Definition and Related compounds
Expert Committee(s): MD-OOD
No. of Commenters: 2
Comment Summary: One commenter suggested deleting “Sterile” from the definition to make it consistent with other USP “Injection” monograph definitions.
Response: Comment incorporated.
Comment Summary: A commenter requested USP clarify whether both related compounds tests are required. A commenter also suggested that Mobile phase be used when diluting the Test solution in Related compounds test 2.
Response: Comments incorporated.

Monograph/Section(s): Galantamine Hydrobromide/Multiple Sections
Expert Committee(s): MD-PP
No. of Commenters: 4
Comment Summary #1: Three commenters requested the removal of Limit of Palladium test.

Response: Comment not incorporated, but the Expert Committee made the Limit of Palladium an optional test.
Comment Summary #2: Two commenters requested the addition of a chiral HPLC method for the Limit of 4*R*, 8*R* Stereoisomer test with an increased limit for the 4*R*,8*R* stereoisomer.
Response: Comment not incorporated at this time. The Committee will publish the HPLC method in *PF* for public comment.
Comment Summary #3: Two commenters requested that limits be added for two additional specified impurities.
Response: Comment not incorporated.

Monograph/Section(s): Glimepiride Tablets/Dissolution
Expert Committee(s): MD-GRE and BPC
No. of Commenters: 1
Comment Summary: The commenter requested an alternate Dissolution test be added to the monograph.
Response: Comment incorporated. As an interim measure, the monograph is becoming official without a Dissolution section. The Committee is working to incorporate the necessary Dissolution tests in an expedited manner.

Monograph/Section(s): Ipratropium Bromide/Limit of ipratropium related compound A and Related compounds
Expert Committee(s): MD-PS
Expert Committee-initiated change: The Expert Committee eliminated the use of an adsorbent with a fluorescent indicator for determining the Limit of ipratropium related compound A. The Committee also removed the 0.05% atropic acid limit in the Related compounds test. That impurity should be treated as an unknown impurity.

Monograph/Section(s): Levalbuterol Hydrochloride/Multiple Sections
Expert Committee(s): AER
No. of Commenters: 3
Comment Summary #1: Comments suggested removal of the test for Color of 1% Solution as performed per General Test Chapter <631>.because it does not add value, particularly in the presence of a test for impurities.
Response: Comment incorporated.
Comment Summary #2: Commenter suggested changing the Residue on ignition limit from “0.10%” to “0.1%.”
Response: Comment incorporated.
Comment Summary #3: One commenter suggested deferring the Related compounds test until the USP RS is available. Another commenter indicated the monograph has tighter limits than ICH for some solvents and requested that the monograph be revised to eliminate reference to specific solvents and their limits.
Response: Both comments incorporated. The committee agreed to defer the section on residual solvents until a suitable method is developed.

Comment Summary #4: A request was received to revise the upper pH range from 5.5 to 5.7.
Response: Comment not incorporated. The current pH range is supported by data.
Comment Summary #5: A request was received to change the limit in the Water test from NMT 0.3% to NMT 1%.
Response: Comment not incorporated because moisture uptake can be controlled with proper packaging.
Comment Summary #6: Commenter requested changing (S) albuterol specifications in the test for Enantiomeric Purity/Chiral ID to from “0.2%” to “1.0%”.
Response: Comment not incorporated because the current lower limit for (S) albuterol is needed to ensure the drug product will meet the required specifications through expiry.
Comment Summary #7: A commenter suggested using one method for both the Assay and Related compounds tests.
Response: Comment not incorporated, but the Related compounds test is being deferred until a suitable method is developed. The Expert Committee is willing to consider future changes to this monograph.

Monograph/Section(s): Levalbuterol Inhalation Solution/Multiple Sections
Expert Committee(s): AER
No. of Commenters: 3
Comment Summary #1: It was suggested to replace the test for Color as performed per General Test Chapter <631> with more common Color and clarity of solution test procedures.
Response: Comment incorporated
Comment Summary #2: A commenter suggested deferring the Related compounds test until the USP RS is available.
Response: Comment incorporated.
Comment Summary #3: A commenter suggested replacing the Uniformity of dosage unit requirement with a test for Minimum Fill.
Response: Comment not incorporated. The results generated from chapter <905> could also be used for minimum fill requirements without the need to perform additional tests.
Comment Summary #4: A commenter suggested including tests for Osmolality and Delivered volume because these are important factors in determining the functional capabilities of inhalation products.
Response: Comments incorporated. The Osmolality test is performed per the instruction in General Chapter <785> and the specification is 280–320 mOsm/kg. The requirement for Delivered volume is incorporated into Uniformity of dosage unit test.

Monograph/Section: Levothyroxine Sodium/Related compounds and Assay
Expert Committees: MD-GRE
No. of Commenters: 1
Comment Summary #1: The commenter noted that the current Related compounds method may not be capable of detecting impurities in API obtained using a alternate synthesis route and requested it be replaced with a new method providing better separation between the chromatographic peaks.

Response: Comment not incorporated at this time, but the Expert Committee encourages manufacturers to submit additional impurity methods to detect their specified impurities.
Comment Summary #2: It was suggested the test material will dissolve faster if a small amount of methanolic NaOH is added during sample preparation in the Assay.
Response: Comment incorporated.
Comment Summary #3: One commenter suggested the Levothyroxine Sodium chemical name and information be clarified.
Response: Comment incorporated. The Committee revised the chemical information and included the word "anhydrous" after the molecular weight of the anhydrous form.

Monograph/Section(s): Liothyronine Sodium/Assay
Expert Committee(s): MD-GRE
No. of Commenters: 0
Expert Committee-initiated change: The Expert Committee received a comment for the Levothyroxine Sodium monograph suggesting that the material will dissolve faster when a small amount of methanolic NaOH is used during sample preparation. Because Liothyronine is similar in nature to Levothyroxine Sodium the same "Note" (see Comment #2 under Levothyroxine Sodium) is being incorporated into this monograph.

Monograph/Section(s): Lorazepam/Related compounds
Expert Committee(s): MD-PP
No. of Commenters: 3
Comment Summary #1: Two commenters requested the limit for Related compound C be increased.
Response: Comment incorporated.
Comment Summary #2: One commenter requested that the sample injection volume be lowered from 100 µL to a smaller volume, e.g.,10 µL.
Response: Comment not incorporated due to lack of supporting data.

Monograph/Section(s): Lorazepam Tablets/Related compounds
Expert Committee(s): MD-PP
No. of Commenters: 1
Comment Summary: The commenter requested eliminating the requirement to use a refrigerated centrifuge.
Response: Comment incorporated.

Monograph/Section(s): Octinoxate/Chromatographic purity and Assay
Expert Committee(s): MD-OOD
No. of Commenter: 1
Comment Summary: Commenter suggested replacing peak responses with peak areas for consistency. Commenter also suggested deleting the column efficiency requirement in the Chromatographic system under Assay because by definition the column efficiency is not used for the temperature ramp condition in the gas chromatograph.
Response: Comments incorporated.

Monograph/Section(s): Omeprazole Magnesium/Multiple Sections
Expert Committee(s): MD-GRE
No. of Commenters: 4
Comment Summary #1: A commenter suggested that tests for Completeness of solution, Loss on drying, Residue on Ignition and Heavy metals be added to the monograph requirements along with a TLC impurities procedure.
Response: Comments not incorporated. The characteristics that would be measured by adding the Loss on drying, Residue on ignition and TLC impurities tests are measured by other tests in the monograph. Regarding Heavy Metals, the Expert Committee is willing to consider future changes to this monograph upon receipt of supporting data.
Comment Summary #2: A commenter requested changing the molecular formula to more clearly reflect the nature of the drug substance.
Response: Comment not incorporated. The current molecular formula is consistent with similar entries in the USAN Dictionary.
Comment Summary #3: A commenter suggested revising the solubility information in the Description and solubility table.
Response: Comment not incorporated at this time. The information in the Description and solubility table is not considered a monograph requirement. The Expert Committee will consider a revision upon receipt of supporting data.
Comment Summary #4: The commenter requested changes to Identification test B.
Response: Comment incorporated.
Comment Summary #5: A commenter reported difficulties meeting system suitability requirements for capacity factor.
Response: The Committee has deleted capacity factor from system suitability requirements because it is not critical to chromatographic separation.
Comment Summary #6: A commenter requested that the Atomic Absorption (AA) spectroscopy methodology in Identification test B and the Assay for magnesium be replaced with a wet chemistry identification test and a titration assay, respectively.
Response: Comment not incorporated. AA spectroscopy is becoming a routine product release analytical method.

Monograph/Section(s): Oxandrolone/Related compounds
Expert Committee(s): MD-PS
Number Commenters: 3
Comment Summary #1: A commenter suggested adding some additional impurities, each to be assigned a limit of 0.1%. The impurities are methyltestosterone, Δ^1-mestalone and an unidentified peak with a retention time of 1.63.
Response: Comment incorporated
Comment Summary #2: A commenter suggested that impurities with relative retention times between 1.09 and 2.14 with relative response factors greater than 1 be identified and the correct relative response factors assigned. In addition, it was recommended to change the detection wavelength from 210 nm to 198 nm so more precise and accurate impurity concentrations may be obtained.
Response: Comments not incorporated due to lack of supporting data.

Monograph/Section(s): Sumatriptan Succinate/Definition
Expert Committee(s): MD-PP
No. of Commenter: 1
Comment Summary: The commenter requested revising the definition to indicate the material is “solvent free”.
Response: Comment incorporated.

Monograph/Section(s): Terbinafine Hydrochloride/Multiple Sections
Expert Committee(s): MD-AA
No. of Commenters: 1
Comment Summary #1: The commenter suggested adding a Melting point test in the monograph for additional characterization.
Response: Comment incorporated.
Comment Summary #2: The commenter suggested including a test for Heavy metals.
Response: Comment not incorporated. A wet chemistry Heavy metals test, as is typical of USP monographs, was not available from the sponsor, and the EC determined that a Heavy metals test is not necessary at this time.
Comment Summary #3: The commenter suggested replacing the Assay titration procedure with an HPLC procedure. The commenter also suggested using the HPLC results as an additional identification test.
Response: Comment not incorporated at this time. The Expert Committee believes that an HPLC method for Assay is desirable, and is willing to consider future changes to this monograph.
Comment Summary #4: The commenter pointed out that the Related compound specifications differ from some approved drug products.
Response: The Committee will consider a revision to the Related compounds specification upon receipt of a Request for Revision and supporting data.
Comment Summary #5: The commenter asked why dehydrated alcohol was specified as a solvent for the Chloride test.
Response: USP General Chapter <191> does not specify the solvent for this test. Because the material is insoluble in water, the Committee felt that the direction to use dehydrated alcohol would be useful.

Monograph/Section(s): Topiramate/Multiple Sections
Expert Committee(s): MD-PP
No. of Commenters: 2
Comment Summary #1: One commenter requested using a range of concentrations rather than a single concentration for Specific Rotation Test.
Response: Comment incorporated.
Comment Summary #2: One commenter requested that the total impurities specification be changed to be the sum of the results obtained from the Related Compounds by TLC and Related Compounds by HPLC tests.
Response: Comment not incorporated due to the possibility of counting the same impurities twice.
Comment Summary #3: One commenter requested to increase the Heavy metals limit to 0.002%.
Response: Comment not incorporated due to lack of supporting data.

Comment Summary #4: One commenter requested inclusion of a separate test for determining fructose levels using refractive index detection.
Response: Comment not incorporated because the current test for Related Compounds by HPLC has adequate selectivity to quantify fructose.
Comment Summary #5: One commenter requested inclusion of a reference standard for Related Compounds by TLC test.
Response: Comment not incorporated at this time.
Comment Summary #6: One commenter requested changing the Standard solution preparation solvent from "water" to "diluent" in the Sulfate/Sulfamate test.
Response: Comment incorporated.

General Chapters

Monograph/Section: <1058> Analytical Instrument Qualification/Multiple Sections
Expert Committee: GC
No. of Commenters: 9
Comments on Introduction:
Comment Summary #1: A comment suggested that the title selected for this chapter is limited to qualification of "instruments" while the document itself covers the qualification of equipment and automated/computerized analytical systems.
Response: Comment incorporated by adding a clarification at the beginning of the chapter indicating that the chapter applies equally to equipment and computerized analytical systems.
Comments on Components of Data Quality:
Comment Summary #2: A commenter indicated that this section is not necessary and the chapter should focus only on AIQ.
Response: Comment not incorporated. The Committee believes that this section helps to define the context of AIQ.
Comment Summary #3: A commenter suggested that the word "base" should not be replaced by "basis". AIQ is not the basis for generating quality data but is merely the base on which other components are placed.
Response: Comment incorporated
Comment Summary #4: A commenter suggested including the concept of calibration as a component of data quality.
Response: Comment not incorporated. The Committee understands that calibration is a core activity in the qualification process.
Comment Summary #5: A commenter suggested changing the definition of validation to the following: "Validation is the collection of documented evidence that an analytical procedure meets pre-determined acceptance criteria for method parameters critical to monograph performance".
Response: Comment not incorporated. The Committee decided to keep the proposed definition for its simplicity and clarity.
Comment Summary #6: It was suggested that the second paragraph under Quality Control Check Samples presents too much detail. The focus of this section should be to describe how these additional activities (method validation, suitability and check samples) are part of a total quality system.
Response: Comment incorporated and a substantial potion of this section was deleted.

Comments on Analytical Instrument Qualification Process:

Comment Summary #7: A commenter suggested adding an element of vendor assessment to Design Qualification.

Response: Comment incorporated.

Comment Summary #8: Several commenters indicated that, in their view, the chapter mandates formal processes and documentation in order to determine the manufacturer's capability for support installation, services, and training.

Response: Comment not incorporated. Because of the informational nature of this chapter, these activities represent current good practice but are not required.

Comment Summary #9: A commenter recommend adding the statement "If the instrument manufacturer's quality practices are inadequate, the user must determine acceptability of the instrument, as well as mitigating activities to reduce risks to an acceptable level for its intended use" to accommodate the special circumstance in which an instrument is only available from a single source that may have deficiencies in their quality system.

Response: Comment not incorporated. Determining the suitability of an analytical instrument supplier is the responsibility of the purchasing company.

Comment Summary #10: Under Installation Qualification, a commenter indicated that installation packages purchased from the manufacturer should be sufficient to comply with IQ without additional user's evaluation.

Response: Comment not incorporated. The word "may" used in the text provides the necessary flexibility.

Comment Summary #11: A commenter indicated that documenting abnormal events observed during assembly is not necessary if standard procedures are followed.

Response: Comment not incorporated. The EC believes any abnormal event occurring during the qualification process needs to be documented.

Comment Summary #12: It was suggested that the assembly and installation section precede the network connection sections because the instruments/systems cannot be connected to the network before they are assembled and installed.

Response: Comment incorporated. The order of these subsections has been reversed.

Comment Summary #13: Under Installation Qualification - Installation Verification, a commenter suggested deleting the sentence "Before proceeding to the next qualification phase, confirm that the IQ has been successfully completed." Formal approvals could delay the process. Previous versions gave more flexibility.

Response: Comment incorporated.

Comment Summary #14: Under Operational Qualification a commenter indicated that the last sentence in the first paragraph is unclear.

Response: Comment incorporated.

Comment Summary #15: In the Operational Qualification section, under Secure Data Storage, Backup, and Archiving, a commenter recommended modifying the statement to include audit trails.

Response: Comment incorporated.

Comment Summary #16: Regarding the Operational Qualification section under Instrument functions, several commenters indicated that not all of the manufacturer's specifications need to be tested if the user requirements only cover a portion of the functionality.

Response: Comment incorporated. The sentence “and required by the user” is reintroduced.
Comment Summary #17: A commenter suggested that the need for OQ after moving an instrument should be considered under Change Control.
Response: Comment not incorporated. An assessment of the suitability of an instrument for continued use after it has been relocated is the responsibility of the company.
Comment Summary #18: A commenter suggested deleting the section Operational Verification because there may be cases when partial PQ is performed before OQ has been finalized.
Response: Comment incorporated.
Comment Summary #19: Under Performance Qualification, a commenter suggested indicating that qualification may be modular or holistic without indicating any preference.
Response: Comment incorporated.
Comment Summary #20: A commenter suggested that PQ intervals need to be determined by the user as defined by individual needs, and that the suggested intervals are not appropriate and may not be suitable for all instruments.
Response: Comment incorporated.
Comment Summary #21: Table 1. In the Performance Qualification column, under Activities, a commenter indicated that the establishment of practices for operation, calibration, maintenance, and change control is part of Installation Qualification and suggest that the statement be moved under that section.
Response: Comment not incorporated. The EC considered that some instruments’ details may not be in place until PQ is performed.
Comment Summary #22: Table 1. A commenter suggested that it is not necessary to repeat PQ, and that periodic calibration should be sufficient for determining the continued suitability of an instrument. Performance Qualification should be performed after the Operational Qualification of an instrument that has undergone a major repair.
Response: Comment not incorporated.
Comments on Roles and Responsibilities:
Comment Summary #23: In the Roles and Responsibilities section, under Users, a commenter suggested revising the second sentence to include the instrument specialists that perform the metrology function existing in many companies.
Response: Comment incorporated.
Comment Summary #24: Under Roles and Responsibilities – Manufacturers it was suggested to delete the references to software validation because the topic is discussed in a specific section of the chapter
Response: Comment incorporated.
Comments on Software Validation:
Comment Summary #25: A commenter suggested that the firmware identity and/or version should be recorded, when possible.
Response: Comment incorporated.
Comment Summary #26: A commenter indicated that the guidance doesn’t clearly define “stand-alone” software.
Response: Comment not incorporated. The EC considered that the term “stand-alone” is self defining.

Comments on Change Control:
Comment Summary #27: A commenter suggested deleting the section on Change Control because it is a separate process from AIQ.
Response: Comment not incorporated. The Expert Committee didn't agree with this suggestion.
Comment Summary #28: Under Change Control, the chapter states that "Change control follows the DQ/IQ/OQ/PQ classification process." A commenter suggested that this not be mandated. Some changes that are covered under change control only need specific or limited tests to demonstrate continued performance, and do not necessarily need formal DQ/IQ/OQ/PQ.
Response: Comment incorporated.
Comments on Instrument Categories:
Comment Summary # 29: Several commenters suggested including clear definitions for instrument categories.
Response: Comments incorporated.
Comment Summary # 30: A commenter suggested moving Densitometers from group C to group B.
Response: Comment not incorporated. A densitometer could be a complex instrument depending on the application.

Monograph/Section: <55> Biological Indicators - Resistance Performance Tests
Expert Committee: MSA
No. of Commenters: 3
Comments on Total Viable Spore Count:
Comment Summary #1: A commenter suggested that population recovery processes for materials other than paper require ultrasonication or mechanical shaking times greater than 5 minutes to remove inoculated spores.
Response: Comment incorporated**.**
Comment Summary #2: A commenter suggested that if an average number of viable spores per carrier is recovered "within -50% and +300% of the labeled counter per carrier" then the indicator should be deemed acceptable.
Response: Comment incorporated.
Comments on D-Value Determination
Comment Summary #3: A commenter suggested replacing the word "controls" with "monitors" when discussing equipment used for gaseous D-Value determinations. The equipment used to create some gaseous sterilants varies and it is more appropriate to indicate the ranges that are observed during D value determinations.
Response: Comment incorporated.
Comment Summary #4: A comment suggested that, where the technology is available, the test chamber should be equipped with monitoring devices for temperature, pressure, humidification, and gas concentration.
Response: Comment incorporated.
Expert Committee-initiated change to delete C.sporogenes:
Clostridium sporogenes BI's are not commercially available.

Expert Committee-initiated change to the sub-section on Apparatus:
Specific apparatus details have been deleted and replaced with the appropriate references that provide the necessary technical content.
Expert Committee-initiated change to the sub-section on Procedure:
The committee has eliminated test procedure details for use of BIER vessels for evaluating microbial resistance. The procedures for BIER vessels are the subject of ISO standards which are included as references.
Expert Committee-initiated change to the sub-section on Recovery:
The revised text allows for the inclusion of additional biological indicator strains.
Expert Committee-initiated change to the sub-section on Calculation:
Details for calculation using the Limited Spearman-Karber method have been deleted because there are at least 3 methods that are in common usage and widely available in the literature in substantially greater detail.
Expert Committee-initiated change to the sub-section on Survival Time-Kill Time:
This section was revised to align it with other revisions to other sub-sections of this chapter as well as to the BI monographs that have been adopted in the USP.