Commentary – *First Supplement to USP 34-NF 29*

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

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No comments were received for the following proposals:

General Chapters
<729> Globule Size Distribution in Lipid Injectable Emulsions
<1010> Analytical Data -- Interpretation and Treatment
<1101> Medicine Dropper
<1601> Products for Nebulization -- Characterization Tests
<1221> Teaspoon

Monographs
Abacavir Oral Solution
Abacavir Tablets
Ademetionine Disulfate Tosylate
Amlodipine Besylate Tablets

No comments were received for the following proposals (continued):

Monographs (continued)
Ascorbyl Palmitate
Bacteriostatic Sodium Chloride Injection
Bupropion Hydrochloride
Cefadroxil for Oral Suspension
Cefdinir Capsules
Entacapone Tablets
Flecainide Acetate Oral Suspension
Forskohlii
Powdered Forskohlii
Powdered Forskohlii Extract
Irbesartan and Hydrochlorothiazide Tablets
Levalbuterol Hydrochloride
Losartan Potassium Tablets
Minocycline Periodontal System
Olanzapine and Fluoxetine Capsules
Pentobarbital Oral Solution
Pentobarbital Sodium Capsules
Raloxifene Hydrochloride Tablets
Repaglinide
Scaffold Human Dermis
Secobarbital Oral Solution
Succinic Acid
Theophylline Oral Suspension
Topiramate

General Chapters

General Chapter: <197> Spectrophotometric Identification Tests
Expert Committee: General Chapters—Chemical Analysis
No. of Commenters: 2
Comment Summary #1: The commenter suggested making the wording for <197D> less prescriptive to include techniques like liquid sample deposition on particles or the silicon carbide abrasive paper.
Response: Comment not incorporated. The Expert Committee considered that liquid deposition could be included in specific monographs when appropriate. However, the abrasive paper technique, used for non-powered samples, is not commonly used in pharmaceutical quality control laboratories.
Comment Summary #2: The commenter indicated that the description for <197D> is very similar to <197K> and can create confusion.
Response: Comment not incorporated. The Expert Committee understands that the definitions are similar. However, it is not appropriate to introduce a change in <197K> via commentary, as this would be a high impact revision meriting public discussion through the *PF* process.

Comment Summary #3: The commenter suggested that <197D> should be added to the list of methods where <197A> and <197E> are suitable alternatives.
Response: Comment not incorporated. The Expert Committee decided to evaluate this proposal in a future revision since it pertains to a portion of the General Chapter not directly affected by the proposed revision.

General Chapter/Section: <563> Identification of Articles of Botanical Origin/ Scanning Electron Microscopy
Expert Committee: General Chapters—Chemical Analysis
Expert Committee-initiated Change: The Expert Committee deleted the last sentence "Although SEM typically yields black and white images, attempts have been made to use low-vacuum SEM to insulate specimens without a metal coating in order to preserve the color information on their surfaces."

General Chapter/Section: <921> Water Determination/Method Ia (Direct Titration)
Expert Committee: General Chapters—Chemical Analysis (GCCA2010)
No. of Commenters: 1
Comment Summary #1: The commenter suggested that there is no justification to limit the range of used volume to between 10% and 100% of the capacity of the burette in the *Test Preparation* when using modern instrumental method endpoint determinations.
Response: Comment not incorporated because this text was not one of the recommended changes in this revision. The Expert Committee will consider revising this General Chapter to incorporate a sentence allowing the use of volumes outside of the established ranges, provided the equipment has been appropriately qualified to operate in this way.
Comment Summary #2: The commenter suggested that Footnote 1 under *Standardization of the Reagent* is inconsistent with the earlier text.
Response: Comment not incorporated because this text was not one of the recommended changes in this revision. Ranges for the use of "*Purified Water* or water standards" are different of those for Sodium tartrate dihydrate standard because of minimum reliable weight and solubility in methanol. The Expert Committee will consider revising this General Chapter to introduce additional clarification.
Comment Summary #3: The commenter suggested that "sodium tartrate dihydrate" should be used consistently instead of "sodium tartrate" under *Standardization of the Reagent*.
Response: Comment incorporated.

General Chapter: <1084> Glycoprotein and Glycan Analysis – General Considerations
Expert Committee: General Chapters—Biological Analysis
No. of Commenters: 5
Comment Summary #1: Several commenters indicated an inconsistent use of nomenclature in describing both glycan structures and linkages throughout the document, including figures and tables
Response: Comments incorporated.

Comment Summary #2: Several commenters suggested improving the clarity and readability of the figures.
Response: Comments incorporated.
Comment Summary #3: Several commenters indicated there were linkage errors in Figure 1.
Response: Comments incorporated.
Comment Summary #4: In the section *Glycan Analysis for Glycosylated Biological Drugs*, several comments focused on the use of glycan analysis as a stability-indicating method or as a measure of process control. The comments indicated a need for clarification in this section.
Response: Comments incorporated.
Comment Summary #5: Several commenters suggested slight wording adjustments to Figure 3A.
Response: Comments incorporated.
Comment summary #6: Several commenters suggested moving the section on labeling of glycans after the HPAEC-PAD section and moving the profiling section before the derivatization section.
Response: Comments incorporated.

General Chapter: <1097> Bulk Powder Sampling Procedures
Expert Committee: Statistics
No. of Commenters: 3
Comment Summary #1: The commenter indicated that under "Types of Systems and General Considerations, Heterogeneous Systems," it is stated that, "The operator should visually inspect the powder bed through its depth before emptying the sampling thief." The commenter indicated that the powder bed cannot be inspected below the surface without disturbing the powder bed. For a heterogeneous material, disturbance of the powder bed may invalidate the sample that has been taken. Therefore, the commenter recommended that this direction be clarified or deleted.
Response: Comment not incorporated. While it is not possible or desirable to inspect the bed after withdrawal of the thief, thief samples provide an opportunity to inspect the bed through its depth if multiple samples at different depths have been taken. Prior to combining the samples (if they are mixed), each should be inspected for possible voids (insufficient filling of one or more compartments) and appearance (similar particle size distribution in all compartments) that may indicate sampling bias or stratification.
Comment Summary #2: The commenter suggested that further clarification should be added to indicate when the use of sqrN+1 is considered inappropriate.
Response: Comment incorporated.
Comment Summary #3: The commenter suggested incorporating a section that provides an overview of definitions used in this field.
Response: Comment incorporated.
Comment Summary #4: The commenter suggested adding more information concerning the potential for contribution to variance if practices used for sub-sampling or compositing are not sound.
Response: Comment not incorporated. The contribution of sub-sampling and compositing to variance is context-specific, so all situations cannot be addressed

specifically in the General Chapter. The contribution of handling errors is covered (at least statistically) in equation 4 as preparation variance. Various methods to reduce preparation errors are covered adequately under the section "Dry Analysis Methods" and that the sub-sampling contributions to variance are adequately covered for a number of specific scenarios in Appendix I.
Comment Summary #5: The commenter suggested that the inclusion of equation (2) is not clear, since it is not referenced further in the text or any examples.
Response: Comment incorporated.
Comment Summary #6: The commenter suggested that the terms in equation 3 should be clarified and placed within context.
Response: Comment incorporated.
Comment Summary #7: The commenter indicated that the scope of the document is unclear, and that there should be a declaration of scope to clarify the General Chapter's intention and what materials it applies to.
Response: Comment incorporated.
Comment Summary #8: The commenter suggested using the word "ideal" instead of "correct" when referring to the sampling process.
Response: Comment incorporated.
Comment Summary #9: The commenter suggested that on page 762, paragraph 3, line 7, the edit for "maximum" to "nominal" may be too vague as it implies a *de facto* standard rather than a measurement.
Response: Comment incorporated.
Expert Committee-initiated Change #1: Several minor corrections were made throughout the text.

General Chapter/Sections: <1180> Human Plasma/All sections
Expert Committee: General Chapters—Biological Analysis
No. of Commenters: 1
All Sections
Comment Summary #1: The commenter suggested that the document would be more concise if information regarding plasma for transfusion and plasma for fractionation were separated. The commenter indicated that, in general, when plasma is collected it has one purpose and regulations are specific to that purpose. Creating two separate information chapters would recognize the differences of these two components.
Response: Comment not incorporated since it would mean a major restructuring of the General Chapter. The Expert Committee will consider this recommendation for a future General Chapter revision.
Comment Summary #2: The commenter suggested stating the scope of the General Chapter is for plasma produced for use in the U.S. The use of plasma in other countries and their regulations should be discussed in a separate section.
Response: Comment not incorporated since the intent of the General Chapter is to give a comprehensive overview.

Overview
Comment Summary #3: The commenter indicated that the products coming from Fraction III do not exist and suggested including fractions from the Kistler-Nitschmann method of manufacture also be included.
Response: Comment not incorporated. The Expert Committee will consider this recommendation as a future revision.
Comment Summary #4: The commenter suggested providing supporting reference for specific limits for residual RBCs, leukocytes, and platelets in the plasma for fractionation. The commenter indicated that there are no criteria for residual red cells in plasma and is strictly a manufacturer's requirement.
Response: Comment incorporated.

Plasma Safety Considerations
Comment Summary #5: The commenter suggested rewording the paragraph on the PPTA's viral marker standard to lend clarity.
Response: Comment incorporated.
Comment Summary #6: The commenter suggested clarifying donor requirements for the serological test for Syphilis.
Response: Comment incorporated.
Comment Summary #7: The commenter suggested revising the size of the minipools to include up to 512 members.
Response: Comment incorporated.
Comment Summary #8: The commenter indicated that the Quarantine section confuses the 60-day hold with quarantine and suggested clarification of these terms.
Response: Comment incorporated and the title of the section has been revised to "Quarantine and Inventory Hold."

Glossary
Comment Summary #9: The commenter suggested clarification for terms "*Blood Component, Blood Establishment* and *Donation Minipool.*"
Response: Comment incorporated.

Appendix I
Comment Summary #10: The commenter indicated the Australia references are incorrect and should be updated.
Response: Comment incorporated.
Comment Summary #11: The commenter suggested replacing the term *Applicant Plasma* with *Applicant Donor*, and clarifying the definition for the term *Plasma for Fractionation*.
Response: Comment incorporated.

Appendix II
Comment Summary #12: The commenter suggested correcting the acceptable blood pressure range for Diastolic to 60-90 mmHg.
Response: Comment incorporated.

Monographs

Monograph/Section: Abacavir Sulfate */*Organic Impurities
Expert Committee: Monographs–Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested to change the relative retention time of descyclopropyl abacavir from 0.54 to 0.65 based on supporting data.
Response: Comment incorporated.

Monograph/Section: Alprazolam Extended Release Tablets/Dissolution
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 2
Comment Summary #1: The commenters requested the inclusion of the *Dissolution* tests for their FDA-approved products.
Response: Comment not incorporated*.* The Expert Committee will consider adding new *Dissolution* tests in the future via the Accelerated Revision Process.
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Monograph/Sections: Citalopram Oral Solution/Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 2
Comment Summary #1: Two commenters requested modifying the *Assay* acceptance criteria from 90.0%–105.0% to 90.0–110.0% to be consistent with the FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #2: The commenter requested widening acceptance criteria for *pH* from 4.0–7.0 to 3.5–7.0 to be consistent with the FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #3: The commenter requested revising the limit for ”any individual unspecified degradation product” under *Organic impurities* from NMT 0.10% to NMT 0.15% to be consistent with the FDA-approved specifications.
Response: Comment incorporated
Comment Summary #4: The commenter requested widening the limit for *Total yeast count* under *Microbial Enumeration Tests and Tests for Specified Microorganisms* from 10 cfu/mL to 50 cfu/mL to be consistent with the FDA-approved specifications.
Response: Comment incorporated.

Monograph/Sections: Divalproex Sodium Delayed–Release Capsules/Dissolution, Labeling
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 2

Comment Summary #1: The commenter requested the inclusion of the *Dissolution* test for the FDA-approved product.
Response: Comment not incorporated**.** The Expert Committee will consider adding this new *Dissolution* test in the future via the Accelerated Revision Process.
Comment Summary #2: The commenter requested the addition of the following *Labeling* statement: "Divalproex Delayed Release Capsules may be swallowed whole or may be administered by carefully opening the Capsule and sprinkling the entire contents on a small amount of soft food. This drug/food mixture should be swallowed immediately and not chewed. It should not be stored for future use."
Response: Comment incorporated.

Monograph/Sections: Divalproex Sodium Extended Release Tablets/Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 2
Comment Summary #1: The commenters requested the inclusion of the *Dissolution* tests for their FDA-approved products.
Response: Comment not incorporated**.** The Expert Committee will consider adding new *Dissolution* tests in the future via the Accelerated Revision Process.
Comment Summary #2: The commenter requested adding a procedure for *Organic Impurities* to the monograph.
Response: Comment not incorporated because the impurities monitored by the commenter are process impurities, and they are already controlled in the drug substance monograph.

Monograph/Sections: Donepezil Hydrochloride Orally Disintegrating Tablets/ Definition, Assay
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter requested tightening the *Assay* acceptance criteria from 90.0%–110.0% to 93.0%–107.0% to reflect the FDA–approved specifications.
Response: Comment incorporated.

Monograph/Sections: Donepezil Hydrochloride Tablets /Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 2
Comment Summary #1: The commenter requested tightening the *Assay* acceptance criteria from 90.0%–110.0% to 93.0%–107.0% to reflect the FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #2: The commenter indicated that one of the impurities in their product is not separated from the analyte by the procedure proposed under *Organic Impurities.*
Response: Comment not incorporated because the commenter's product has not yet received full FDA approval. The Expert Committee will consider addressing this

comment via a Pending revision to the monograph as part of the *USP Pending Monographs* initiative.

Monograph/Sections: Drospirenone/Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 5
Comment Summary #1: The commenter requested that the system suitability requirement for the signal-to-noise ratio be removed from the *Assay* procedure.
Response. Comment not incorporated. The Expert Committee will consider this request in a future PF publication.
Comment Summary #2: The commenter requested replacing the gradient elution procedure in the *Assay* with the isocratic procedure.
Response. Comment not incorporated. The Expert Committee will consider this request in a future PF publication.
Comment Summary #3: The commenter requested replacing the HPLC *Assay* procedure with the one described under *Organic Impurities* Procedure 2 to simplify the analysis of drospirenone.
Response. Comment not incorporated. The Expert Committee will consider this request in a future PF publication.
Comment Summary #4: The commenter requested that the proposal be deferred from the *First Supplement to USP 34–NF 29* because reference standard materials for the impurities listed in the monograph are not available for evaluation.
Response: Comment not incorporated. The Expert Committee considers the information available in the monograph sufficient for the procedure to be properly executed.
Comment Summary #5: The commenter requested that 6,7-epidrospirenone impurity be added under the *Organic Impurities, Procedure 2* with a limit of NMT 0.1%, to reflect the commenter's FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #6: The commenter requested that the limits for individual impurities under the *Organic Impurities, Procedure 2* be changed from NMT 0.10% to NMT 0.1%, and the total impurity limits be changed from NMT 0.3% to NMT 0.4%, to reflect the commenter's FDA-approved specifications.
Response: Comment incorporated.
Comment summary #7: The commenters indicated that the impurity profile of the drug substance manufactured by their companies is different from the profile included in the *PF* proposal, and the proposed *PF* procedure does not separate their impurities.
Response: Comment not incorporated because the commenters' products have not yet received full FDA approval. The Expert Committee will consider addressing this comment via a Pending revision to the monograph as part of the *USP Pending Monographs* initiative.
Comment Summary #8: The commenter requested widening the limit for drospirenone related compound A under the *Organic Impurities, Procedure 2* from NMT 0.10% to NMT 0.15%.
Response: Comment not incorporated because the commenter's product has not yet received full FDA approval. The Expert Committee will consider addressing this

comment via a Pending revision to the monograph as part of the *USP Pending Monographs* initiative.
Comment Summary #9: The commenter indicated that the 5–hydroxydrospirenone impurity is unstable, and requested that the specification for this impurity be removed from the *Organic Impurities, Procedure 2*.
Response: Comment not incorporated. The validation data from the sponsor do not indicate that this impurity is unstable.
Comment Summary #10: The commenter indicated that several impurities may co–elute when the HPLC column, used for the development and validation of the procedure, is operated at the temperature of 35°, which is specified in *Organic Impurities, Procedure 2*. The commenter requested expanding the column temperature range to 40°, and adding YMC Pack ODS AQ column as an alternative column.
Response: Comment incorporated.
Comment Summary #11: The commenter suggested that an isocratic step from 0–2 minutes be added to the mobile phase gradient under *Organic Impurities, Procedure 2*, to match that in the *European Pharmacopoeia*.
Response: Comment incorporated.
Comment Summary #12: The commenter requested that 20º be specified as the temperature for the *Specific rotation* test, based on supporting data.
Response: Comment incorporated.

Monograph/Section: Efavirenz/Organic Impurities
Expert Committee: Monographs– Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested to identify efavirenz ethane analog impurity as efavirenz related compound B for further clarification.
Response: Comment incorporated.
Comment Summary #2: The commenter suggested adding equilibration time to the gradient table in the *Procedure 2*, based on supporting data.
Response: Comment incorporated.

Monograph/Section: Efavirenz Capsules/Organic Impurities
Expert Committee: Monographs– Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested changing the acceptance criterion for efavirenz aminoalcohol from NMT 0.15% to NMT 0.25% to be consistent with the sponsor's FDA-approved specifications.
Response: Comment incorporated.

Monograph/Sections: Entacapone/Heavy Metals/Description and Solubility
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter requested specifying *Method II* under the *Heavy Metals* test.
Response: Comment incorporated.

Comment Summary #2: The commenter requested the revision of the solubility portion of the *Description and Solubility*.
Response: Comment not incorporated. The Expert Committee will consider these changes once the commenter's product receives full FDA approval.

Monograph/Section: Escitalopram Oxalate/Water Determination
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter suggested revising the specifications for *Water Determination* from NMT1.0% to NMT1.5%, to make them consistent with the *Authorized USP Pending monograph* for Escitalopram Oxalate.
Response: Comment not incorporated. The Expert Committee will consider these changes once the commenter's product receives full FDA approval.

Monograph/Section: Fludarabine Phosphate Injection/Organic Impurities
Expert Committee: Monographs–Small Molecules 3
Expert Committee–initiated Change #1: It is clarified that *Early Eluting Impurities* and *Late Eluting Impurities* are the impurities eluting before and after the fludarabine peak, respectively.
Expert Committee–initiated Change #2: The term "monitored" in the statement "it is a process impurity monitored in the drug substance monograph" is changed to "controlled."

Monograph/Sections: Hydrochlorothiazide Capsules/Multiple Sections
Expert Committee: Monographs–Small Molecules 2
No. of Commenters: 1
Comment Summary #1: The commenter suggested adding an *Identification* test based on the infrared absorption.
Response: Comment not incorporated. The Expert Committee is willing to consider future changes to the monograph upon receipt of the necessary supporting data.
Comment summary # 2: The commenter requested revising the limit for "any other individual impurity" from NMT 0.1% to NMT 0.2% under *Organic impurities* to be in accordance with the ICH guidelines.
Response: Comment incorporated.

Monograph/Section: Hydrous Benzoyl Peroxide/Assay
Expert Committee: Monographs– Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested to further clarify that the acceptance criteria under *Assay* are calculated as a percentage of the labeled amount.
Response: Comment incorporated.

Monograph/Section(s): Indinavir Sulfate/Other Components
Expert Committee (s): Monographs– Small Molecules 1
No. of Commenters: 2

Comment Summary #1: The commenters requested that the quantitative test for *Content of Sulfate* not be deleted because the appropriate level of sulfate, as well as detection of bis-sulfate contaminant, are monitored using this test.
Response: Comment incorporated.

Monograph/Sections: Lopinavir /Multiple Sections
Expert Committee: Monographs– Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested reporting the acceptance criteria to one decimal place for all impurities, including "any other individual impurity," under *Organic impurities* to be consistent with the sponsor's FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #2: The commenter requested changing Relative Response Factors (RRF) of greater than 1.0 from one decimal place to two decimal places in the *Impurity Table 1* and *Impurity Table 2*.
Response: Comment not incorporated because it is USP policy to express RRF values in the monographs to two decimal places if less than 1.0 and to one decimal place if equal to or more than 1.0.
Comment Summary #3: The commenter suggested revising *Identification* test from *Infrared Absorption <197S>* to *Infrared Absorption <197A>* to avoid using deuterated chloroform.
Response: Comment not incorporated. The Expert Committee will consider this request in a future *PF* publication.

Monograph/Section: Mefloquine Hydrochloride Tablets/Dissolution
Expert Committee: Monographs–Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested the inclusion of the *Dissolution* test for their FDA-approved product.
Response: Comment not incorporated**.** The Expert Committee will consider adding the new *Dissolution* test in the future via the Accelerated Revision Process.

Monograph/Sections: Midodrine Hydrochloride/Multiple Sections
Expert Committee: Monographs–Small Molecules 2
No. of Commenters: 1
Comment Summary #1: The commenter requested widening the limit of midodrine related compound A from NMT 0.1% to NMT 0.2% under *Organic impurities* to be consistent with the FDA-approved specifications.
Response: Comment incorporated.
Comment Summary #2: The commenter requested widening the limit for *Residue on ignition* from NMT 0.1% to NMT 0.2% to be consistent with the FDA-approved specifications.
Response: Comment incorporated.

Monograph/Section: Midodrine Hydrochloride Tablets/Dissolution
Expert Committee: Monographs–Small Molecules 2

No. of Commenters: 1
Comment Summary #1: The commenter requested the inclusion of the *Dissolution* test for their FDA–approved product.
Response: Comment not incorporated**.** The Expert Committee will consider adding the new *Dissolution* test in the future via the Accelerated Revision Process.

Monograph/Sections: Minocycline Hydrochloride/Multiple Sections
Expert Committee: Monographs–Small Molecules 1
No. of Commenters: 1
Comment Summary #1: The commenter requested specifying that the solution stability statement in the *Organic impurities* test pertains only to the *Standard* and *Sample Solutions*.
Response: Comment incorporated.
Expert Committee–initiated Change #1: A solution stability statement, similar to the one under *Organic impurities*, is also added under the *Assay*.

Monograph/Sections: Pramipexole Dihydrochloride /Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 4
Comment Summary #1: The commenter requested revising the flow rate in the Assay from 1.5 mL/min to 1.8 mL/min to be consistent with the increase in column length from 12.5 cm to 15 cm.
Response: Comment not incorporated. Based on the robustness data, the flow rate is not a critical parameter for this separation.
Comment Summary #2: The commenter requested the concentration of *Standard solution* in the *Organic Impurities* procedure be changed from 7.5 μg/mL to 1.5 μg/mL to be consistent with EP 6.8.
Response: Comment incorporated.
Comment Summary #3: The commenter requested widening the specifications under *Water Determination* from 4.5%–6.5% to 4.5%–7.0%.
Response: Comment not incorporated because the commenter's product has not yet received full FDA approval. The Expert Committee will consider addressing this comment via a Pending revision to the monograph as part of the *USP Pending Monographs* initiative.

Monograph/Sections: Rizatriptan Benzoate/Multiple Sections
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 4
Comment summary #1: The commenter indicated that the *Assay* acceptance criteria are different from the approved limits.
Response. Comment not incorporated because this proposal is a part of the prospective harmonization pilot study.
Comment summary #2: The commenter requested to add a note that *Identification–A* could be performed using <*197A*> or <*197M*>*,* in addition to <*197K*>*.*
Response. Comment incorporated.

Comment summary #3: The commenter requested the relative retention time for benzoic acid be changed from 2.0 to 2.1 to be consistent with the proposal published in *PharmEuropa* 21.4.
Response. Comment incorporated.
Comment summary #4: The commenter recommended using *Solution A* instead of the *Diluent* for the preparation of the *Standard solution* and the *Sample solution* under *Assay* and *Organic Impurities* procedures.
Response. Comment incorporated.
Comment summary #5: The commenter indicated that they were unable to meet the tailing factor requirement of NMT 3.0 under the *Assay*, and requested it to be raised to NMT 3.5.
Response. Comment incorporated.
Comment summary #6: The commenter requested revising the *Sample solution* under *Heavy Metals* to be consistent with the proposal published in *PharmEuropa* 21.4.
Response. Comment incorporated.
Comment summary #7: The commenter requested that the quantitation procedure under *Organic Impurities* procedure be harmonized with *PharmEuropa* 21.4.
Response. Comment not incorporated because this is not consistent with the current USP policy.
Comment summary #8: The commenter recommended adding a system suitability requirement for the signal-to-noise ratio.
Response. Comment incorporated.

Monograph/Section: Ropinirole Tablets/Identification
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter requested that a second Identification test, based on a TLC procedure, be added to the monograph.
Response: Comment not incorporated**.** The Expert Committee considers a single identification test based on HPLC retention time agreement to be adequate for a drug product monograph.

Monograph/Section: Sodium Acetate/Identification
Expert Committee: Monographs–Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter requested to specify that the *Sample solution* for the *Identification–B* is used for the lanthanum nitrate portion of the test under *Identification Tests–General, Acetate.*
Response: Comment incorporated.

Monograph/Sections: Telmisartan and Hydrochlorothiazide Tablets/Multiple Sections
Expert Committee: Monographs–Small Molecules 2
No. of Commenters: 1
Comment Summary #1: The commenter requested tightening the *Assay* acceptance criteria for hydrochlorothiazide.

Response: Comment not incorporated because the proposed acceptance criteria are consistent with the sponsor's FDA-approved specifications.
Comment Summary #2: The commenter requested to adding a test for *Water Determination* to the monograph.
Response: Comment not incorporated because the content of water is formulation-specific.
Comment Summary #3: The commenter requested revising the limits for benzothiadiazine related compound A and the total impurities under *Organic impurities.*
Response: Comment not incorporated because the proposed acceptance criteria are consistent with the sponsor's FDA-approved specifications.

Monograph/Section: Terazosin Capsules/Dissolution
Expert Committee: Monographs–Small Molecules 2
No. of Commenters: 1
Comment Summary #1: The commenter requested correcting the tolerances under *Dissolution Test 1* from "NLT 80%" to "NLT 80% (Q)."
Response: Comment incorporated.

Monograph/Sections: Terazosin Tablets/Multiple Sections
Expert Committee: Monographs–Small Molecules 2
No. of Commenters: 1
Comment Summary #1: The commenter requested revising the *Sample solutions* under *Identification*, *Organic impurities* and *Dissolution* sections to account for the various tablet strengths of the marketed product.
Response: Comment not incorporated. The Expert Committee will consider addressing this comment in a future *PF* publication.
Comment Summary #2: The commenter indicated that modifying the content of triethylamine in the *Mobile phase* and the flow rate may improve the separation under the *Assay*, and requested to include this information in the monograph.
Response: Comment not incorporated. The Expert Committee will consider addressing this comment in a future *PF* publication.
Comment Summary #3: The commenter suggested revising specifications for *Organic impurities* to accommodate their FDA-approved specifications.
Response: Comment not incorporated. The Expert Committee will consider addressing this comment in a future revision.

Monograph/Section: Valacyclovir Tablets/Organic Impurities
Expert Committee: Monographs–Small Molecules 1
No. of Commenters: 3
Comment Summary #1: The commenter requested removing the acceptance criteria for D-valacyclovir because it is a process impurity and is controlled in the drug substance monograph.
Response: Comment incorporated.

Monograph/Section: Zonisamide Capsules/Organic Impurities
Expert Committee: Monographs–Small Molecules 4

No. of Commenters: 1
Comment Summary #1: The commenter requested correcting the chemical name of the impurity eluting at relative retention time of 1.6 from dimethylzonisamide to methylzonisamide.
Response: Comment incorporated.