



Commentary – Second 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

- <1027> Flow Cytometry
- <1046> Cell and Gene Therapy Products
- <1047> Gene Therapy Products
- <2040> Disintegration and Dissolution of Dietary Supplements

Monographs

- Ammonium Molybdate
- Anti-A Blood Grouping Serum
- Anti-B Blood Grouping Serum
- Antihemophilic Factor
- Anti-Human Globulin Serum
- Antivenin (Crotalidae) Polyvalent

No comments received for the following proposals (continued):

Monographs (continued)

Antivenin (Latrodectus Mactans)
Antivenin (Micrurus Fulvius)
Bicalutamide
Blood Grouping Serums
Blood Grouping Serums Anti-D, Anti-C, Anti-E, Anti-C, Anti-E
Botulism Antitoxin
Bromocriptine Mesylate
Bupropion Hydrochloride Extended-Release Tablets
Coccidioidin
Codeine Sulfate
Codeine Sulfate Tablets
Cryoprecipitated Antihemophilic Factor
Diphtheria and Tetanus Toxoids Adsorbed
Divalproex Sodium
Doxycycline Hyclate Delayed-Release Tablets
Ethinodiol Diacetate and Ethinyl Estradiol Tablets
Fluvastatin Sodium
Ganciclovir
Heparin Calcium
Heparin Calcium Injection
Histoplasmin
Hypophosphorous Acid
Influenza Virus Vaccine
Maleic Acid
Measles and Rubella Virus Vaccine Live
Measles Virus Vaccine Live
Measles, Mumps, and Rubella Virus Vaccine Live
Methylethylergonovine Maleate Injection
Mumps Skin Test Antigen
Mumps Virus Vaccine Live
Norethindrone Acetate and Ethinyl Estradiol Tablets
Oxycodone Hydrochloride Extended-Release Tablets
Phenoxybenzamine Hydrochloride Capsules
Platelet Concentrate
Poliovirus Vaccine Inactivated
Whole Blood
Yellow Fever Vaccine
Polyoxyl Lauryl Ether
Propylene Glycol Dicaprylate/Dicaprate
Smallpox Vaccine
Sorbic Acid
Tetanus and Diphtheria Toxoids Adsorbed for Adult Use
Tetanus Toxoid

No comments received for the following proposals (continued):

Monographs (continued)

Tetanus Toxoid Adsorbed
Thrombin
Triamcinolone Acetonide Injectable Suspension
Triamcinolone Hexacetonide
Triamcinolone Hexacetonide Injectable Suspension
Tuberculin
Vitamin A Tablets

General Chapters

General Chapter: <413> Impurities Testing in Medical Gases

Expert Committee(s): General Chapters

No. of Commenters: 2

Comment Summary #1: A commenter suggested that the title of the section was misleading since the General Chapter is limited to describing the use of detector tubes in medical gas impurity analysis.

Response: Comment not incorporated. There are some exceptions, but detector tubes traditionally have been used for determining impurities.

Comment Summary #2: A commenter suggested that it would be clearer to use the gas volume as defined by the manufacturer of the detector tube.

Response: Comment incorporated.

Comment Summary #3: A commenter suggested clarifying the purpose of selecting the proper float setting.

Response: Comment incorporated.

General Chapter/Section(s): <415> Medical Gases Assay

Expert Committee(s): General Chapters

No. of Commenters: 2

Comment Summary #1: A commenter suggested that the sections on Methods, Qualification, Validation, and Procedure were not needed.

Response: Comment not incorporated because this is the new format for USP general chapters.

Comment Summary #2: A commenter suggested that the manufacturer should be clarified in the gas chromatography section.

Response: Comment was incorporated by specifying the GC manufacturer.

Comment Summary #3: A commenter suggested replacing the term 'challenge testing' with the term 'periodic calibration'.

Response: Comment incorporated.

Comment Summary #4: A commenter suggested allowing the use of other recognized standards, because NIST standards are not the only recognized standards.

Response: Comment incorporated.

Comment Summary #5: A commenter indicated that because standard concentrations vary within the proposed monographs, it will be more appropriate to provide nominal concentrations in the certification tolerance for those standards in the Reagents, Indicators, and Solutions section.

Response: Comment incorporated.

Monographs

Monograph/Section(s): Alclometasone Dipropionate/Organic Impurities

Expert Committee: Monographs—Small Molecules 4

No. of Commenters: 1

Comment Summary #1: 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 at this time. The Expert Committee is willing to consider future changes to the monograph upon receipt of the necessary supporting data.

Monograph/Section(s): Amoxicillin Capsules/Microbial Enumeration Tests and Tests for Specified Microorganisms.

Expert Committee: Monographs—Small Molecules 1

No. of Commenters: 2

Comment Summary #1: The commenters requested this test be deleted from the monograph.

Response: Comment not incorporated. The Expert Committee believes that the test is necessary to control product quality.

Monograph/Section(s): Amoxicillin and Clavulanate Potassium Tablets/Microbial Enumeration Tests and Tests for Specified Microorganisms

Expert Committee: Monographs—Small Molecules 1

No. of Commenters: 2

Comment Summary #1: The commenters requested this test be deleted from the monograph.

Response: Comment not incorporated. The Expert Committee believes that the test is necessary to control product quality.

Monograph/Section(s): Amoxicillin and Clavulanate Potassium for Oral Suspension/
Multiple Sections

Expert Committee: Monographs—Small Molecules 1

No. of Commenters: 2

Comment Summary #1: The commenters requested this test be deleted from the monograph.

Response: Comment not incorporated. The Expert Committee believes that the test is necessary to control product quality.

Monograph/Section(s): Amoxicillin for Oral Suspension/Microbial Enumeration Tests and Tests for Specified Microorganisms.

Expert Committee: Monographs - Small Molecules 1

No. of Commenters: 2

Comment Summary #1: The commenters requested this test be deleted from the monograph.

Response: Comment not incorporated. The Expert Committee believes that the test is necessary to control product quality.

Monograph/Section(s): Amoxicillin Tablets/Microbial Enumeration Tests and Tests for Specified Microorganisms

Expert Committee: Monographs—Small Molecules 1

No. of Commenters: 2

Comment Summary #1: The commenters requested this test be deleted from the monograph.

Response: Comment not incorporated. The Expert Committee believes that the test is necessary to control product quality.

Monographs/Section(s): Bacopa and Powdered Bacopa

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Include new identification test A which will state that the article meets the requirements under Specific Tests, Botanic Characteristics; renumber the other identification tests B and C.

Expert Committee-initiated Change #2: Label identification test C with the heading “HPLC Identification Test.”

Expert Committee-initiated Change #3: Modify the Botanic Characteristics description in the monograph for Powdered Bacopa.

Expert Committee-initiated Change #4: Replace the development distance in the TLC identification from about 90% to about three-fourths of the plate.

Expert Committee-initiated Change #5: Correct the particle size of the HPLC column stationary phase to 5 µm.

Monograph/Sections: Centella Asiatica and Powdered Centella Asiatica

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Include new identification test A which will state that the article meets the requirements under Specific Tests, Botanic Characteristics, renumber the other identification tests B and C.

Expert Committee-initiated Change #2: Label identification test C with the heading “HPLC Identification Test.”

Expert Committee-initiated Change #3: Replace the development distance in the TLC identification from about 90% to about three-fourths of the plate.

Expert Committee-initiated Change #4: Revise the labeling section to include the following sentence: This article is exempted from the requirements of the General Notices with respect to pregnancy and lactation statement (section 10.4.50 - Labeling Botanical Containing Products).

Monograph/Sections: Crypthecodinium Cohnii Oil/Multiple Sections

Expert Committee: Monographs—Dietary Supplements

No. of Commenters: 2

Comment Summary #1: The commenter requested changing the *Title* from *Crypthecodinium Cohnii Oil* to DHA Algal Oil (*Crypthecodinium Cohnii*).

Response: Comment not incorporated. The Expert Committee agrees with the previous (2005-2010) DS Expert Committee's decision not to pursue the change. The Committee finds the use of acronyms and parenthesis not appropriate for a pharmacopeial title.

Comment Summary #2: The commenter requested changing the DHA Content expression under the *Definition* from "% (w/w) to mg/g."

Response: Comment not incorporated. In order to match the current industry practice, the labeling section in the monograph requires the article to be labeled in mg/g. The Expert Committee believes the DHA content in the *Definition* should be expressed in % (w/w) to match requirements from regulatory agencies and to maintain consistency with other monographs in USP.

Comment Summary # 3: The commenter requested removing the *Fatty Acid Profile* test under the *Identification* because it is unnecessarily prescriptive and restrictive to define a safe and suitable product. Instead, the commenter suggested the incorporation of the following under the *Identification*: "DHA Algal Oil (*Crypthecodinium Cohnii*) is characterized by significant amounts of long-chain C22 fatty acids. The sum of the area peak for DHA methyl esters is not less than 35%."

Response: Comment not incorporated. The Expert Committee believes the *Fatty Acid profile* test is not unnecessarily prescriptive because the analytical procedure is already carried out for the assay. It is not unnecessarily restrictive because the fatty acid profile is a tool used to characterize the oil source. In this case it allows differentiation from the two currently available algal sources of oils rich in DHA, and from enriched fish sources, which would become undistinguishable if the comment were adopted.

Comment Summary #4: The commenter suggested: (1) The *Fatty Acid Profile* under the *Identification* be changed to *Long Chain Unsaturated Fatty Acid Profile*. (2) A formula for calculation the percentage of individual fatty acids be added to *Fatty Acid Profile*, and (3) The relative retention times for the targeted fatty acids be added to the *Table for Fatty Acid Profile*.

Response: Three comments incorporated.

Comment Summary #5: The commenter requested changing the *Acceptance criteria* for DHA content under *Content of DHA* from NLT 40% to NLT 35%.

Response: Comment incorporated.

Comment Summary #6: The commenter requested changing the unit for the limit of inorganic impurities under *Inorganic Impurities* from µg/g to mg/kg.

Response: Comment not incorporated. The Expert Committee believes that the inorganic impurities limit should be expressed in µg/g to match the unit expression for these types of limits in other USP-NF monographs. The numerical value in µg/g is equivalent to the expression mg/kg and therefore the Expert Committee finds no reason to change it.

Comment Summary #7: The commenter requested changing the label of DHA content in the *Labeling* from mg/g to percentage (%).

Response: Comment not incorporated. The expression in percentage (w/w) is already in the definition to match the regulatory requirements. Therefore, the Expert Committee believes that labeling for the DHA content should be in mg/g to match the industry practice.

Monograph/Section(s): Chitosan/Multiple Sections

Expert Committee(s): Monographs—Excipients

No. of Commenters: 4

Comment Summary #1: In the *Definition*, the commenter suggested that the degree of deacetylation of Chitosan should not be less than 50.0 percent.

Response: Comments not incorporated due to concerns raised by Food and Drug Administration. The Expert Committee clarified the *Definition* to include an upper limit that reflects a range and changed the text to be, “Its degree of deacetylation is not less than 70.0 percent and not more than 95.0 percent.”

Comment Summary #2: In the footnote specifying a supplier of β -glucan blocker, the commenter suggested an additional supplier, Charles River, be added.

Response: Comment incorporated.

Comment Summary #3: In the test for *Limit of lead, mercury, chromium, nickel, cadmium, and arsenic*, the commenter recommended the specifications for lead, mercury, chromium, and arsenic be 0.5, 0.2, 1.0, and 0.5 ppm, respectively, with supporting data.

Response: Comment incorporated.

Comment Summary #4: In the test for *Limit of Iron*, the commenter recommended the blank standard be prepared as directed in the test for *Limit of lead, mercury, chromium, nickel, cadmium, and arsenic*

Response: Comment incorporated.

Comment Summary #5: In the test for *Heavy Metals*, the commenter suggested the specification should be increased from 10 ppm to 40 ppm.

Response: Comments not incorporated due to a lack of supporting data.

Comment Summary #6: In the test for *Average Molecular Weight and Molecular Weight Distribution*, the commenter suggested an alternative method or viscosity test should be used.

Response: Comments not incorporated due to a lack of validation report and data. The Expert Committee will consider and evaluate the alternative method once the supporting data are received. The Expert Committee added the word “apparent” at the beginning of the test title and also introduced a note to indicate that this test is applicable to Chitosan of average molecular weight not more than 1,000,000 Daltons. The note also states that in the following test an apparent average molecular weight is determined.

Comment Summary #7: In the test for *Average Molecular Weight and Molecular Weight Distribution*, the commenter recommended adding a note to state that the resolution between the PEG standard with molecular weight of about 1,000,000 Daltons and its adjacent PEG standard should be not less than 1.0 if 1.7 cannot be met.

Response: Comment incorporated.

Expert Committee-initiated Change #1: In the *Labeling* section, add a text “Label to indicate the natural source from which Chitosan is derived.”

Monograph/Sections: Crypthecondinium Cohnii Oil Capsules
Expert Committee: Monograph—Development Dietary Supplements
Expert Committee-initiated Changes: All the changes to the monograph were made in agreement with the changes proposed/approved for the dietary ingredient monograph. (See comments in Crypthecodinium cohnii Oil.) The sections Strength and Content of DHA were modified for consistency with the acceptance criteria in the Definition.

Monograph/ Section(s): Escitalopram Tablets/Organic Impurities, Dissolution
Expert Committee: Monographs—Small Molecules 4
No. of Commenters: 2
Comment Summary #1: The commenter requested including two additional specified impurities with appropriate limits, and widening the limit for any other individual unspecified impurity from NMT 0.1% to NMT 0.20%.
Response: Comment not incorporated because the commenter's 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 #2: Two commenters requested inclusion of Dissolution tests for their products.
Response: Comment not incorporated. The Expert Committee will consider adding these new Dissolution tests once the commenters' products receive full FDA approval.

Monograph/Section(s): Etomidate/Multiple Sections
Expert Committee: Monographs—Small Molecules 4
No. of Commenters: 1
Comment Summary #1: The commenter requested adding the following tests to the monograph: Identification test by UV spectroscopy, Appearance test, Percent Transmittance in dichloromethane, Microbial Limit test, and Bacterial Endotoxin test.
Response: Comment not incorporated. The Expert Committee considers the proposed specifications to be adequate for the public standard.
Comment Summary #2: The commenter requested including a stereoisomeric purity test to monitor the amount of S-enantiomer.
Response: Comment not incorporated. The Expert Committee is willing to consider replacement of the test for Specific rotation currently included in the monograph with the HPLC test for limit of S-enantiomer upon receipt of the necessary supporting data.
Comment Summary #3: The commenter requested inclusion of two additional specified impurities with appropriate limits.
Response: Comment not incorporated at this time. The Expert Committee is willing to consider future changes to the monograph upon receipt of the necessary supporting data.

Monograph/Section(s): Etomidate Injection/Organic Impurities

Expert Committee: Monographs—Small Molecules 4

No. of Commenters: 3

Comment Summary #1: The commenter requested correcting the relative response factor value for propylene glycol esters from 20.9 to 0.9 in *Impurity Table 2*.

Response: Comment incorporated.

Comment Summary #2: Two commenters indicated that propylene glycol esters, controlled by the *Procedure 2*, could also be detected at the relative retention time of 0.77 under *Procedure 1*. The commenters requested adding propylene glycol esters to the *Impurity Table 1* under *Procedure 1* with a footnote directing the analyst to use *Procedure 2* for quantifying this impurity.

Response: Comment incorporated.

Monographs/Section(s): Garcinia Cambogia and Powdered Garcinia Cambogia

Expert Committee(s): Monograph-Development Dietary Supplements

Expert Committee-initiated Change #1: Include new identification test A which will state that the article meets the requirements under Specific Tests, Botanic Characteristics; renumber the other identification test B.

Expert Committee-initiated Change #2: Label identification test B with the heading “HPLC Identification Test.”

Monographs/Sections: Garcinia Indica and Powdered Garcinia Indica

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Include new identification test A which will state that the article meets the requirements under Specific Tests, Botanic Characteristics; renumber the other identification tests B and C.

Expert Committee-initiated Change #2: Label identification test C with the heading “HPLC Identification Test.”

Expert Committee-initiated Change #3: Replace the development distance in the TLC identification from about 90% to about three-fourths of the plate.

Monograph/Sections: Glutathione/Multiple Sections

Expert Committee: Monographs—Dietary Supplements

No. of Commenters: 1

Comment Summary #1: The commenter requested changing the acceptance criteria for glutathione in the *Definition* and the *Assay* from 98.5% - 101.5% to 98.0% -101.0% in order to be consistent with the JP’s and EP’s glutathione monographs.

Response: Comment incorporated.

Comment Summary #2: The commenter requested correcting the specified temperature under the *Optical Rotation* to 20°C in order to be consistent with the JP’s and EP’s glutathione monographs.

Response: Comment incorporated.

Comment Summary #3: The commenter requested correcting the mobile phase preparation under *Organic Impurities* because of a typo in the pH adjustment.

Response: Comment incorporated.

Comment Summary #4: The commenter questioned about the use of USP L-phenylalanine under the *System suitability solution* instead of D-phenylglycine as being used in the JP's and EP's glutathione monographs.

Response: Comment not incorporated. The USP L-phenylalanine is readily available in the US and its chromatographic performance is similar to D-phenylglycine. The commenter agreed to leave it as is.

Monograph/Section: Homatropine Methylbromide/Chemical Information

Expert Committee: Monographs—Small Molecules 3

Expert Committee–initiated Change: The third chemical name, based on the IUPAC nomenclature, is added to the monograph.

Monograph/Section(s): Hydroxypropyl Corn Starch/Procedure for Hydroxypropyl Groups

Expert Committee(s): Monographs—Excipients

No. of Commenters: 1

Comment Summary #1: The commenter recommended replacing the sentence “Weigh 12.0 mg of this sample” with the text “Determine the moisture content (*B*) on 5 g of the washed and dried starch following the *Loss on Drying* test.”

Response: Comment incorporated.

Monograph/Section(s): Hydroxypropyl Pea Starch/Procedure for Hydroxypropyl Groups

Expert Committee(s): Monographs—Excipients

No. of Commenters: 1

Comment Summary #1: The commenter recommended replacing the sentence “Weigh 12.0 mg of this sample” with the text “Determine the moisture content (*B*) on 5 g of the washed and dried starch following the *Loss on Drying* test.”

Response: Comment incorporated.

Monograph/Section(s): Hydroxypropyl Potato Starch/Procedure for Hydroxypropyl Groups

Expert Committee(s): Monographs—Excipients

No. of Commenters: 1

Comment Summary #1: The commenter recommended replacing the sentence “Weigh 12.0 mg of this sample” with the text “Determine the moisture content (*B*) on 5 g of the washed and dried starch following the *Loss on Drying* test.”

Response: Comment incorporated.

Monograph/Section(s): Lidocaine/Other

Expert Committee: Monographs—Small Molecules 4

No. of Commenters: 1

Comment Summary #1: The commenter indicated that the USP monograph needs further modernization, and requested to add a procedure for *Organic impurities* to the monograph.

Response: Comment not incorporated. The Expert Committee is willing to consider future changes to the monograph upon receipt of the necessary supporting data.

Monograph/Section(s): Lidocaine Hydrochloride/Multiple Sections

Expert Committee: Monographs—Small Molecules 4

No. of Commenters: 1

Comment Summary #1: The commenter indicated that the USP monograph needs further modernization, and requested to add a procedure for *Organic impurities* to the monograph.

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 suggested that the procedure for the *Identification—A* by infrared absorption could be simplified if a USP Lidocaine Hydrochloride RS was available.

Response: Comment not incorporated. The Expert Committee is willing to consider future changes to the monograph upon receipt of the necessary supporting data and when the bulk material for the RS development is provided to support the revision.

Monograph/Section(s): Loxapine Succinate/Organic Impurities

Expert Committee: Monographs—Small Molecules 4

No. of Commenters: 1

Comment Summary #1: The commenter requested including a Note under the *Standard solution* to indicate that USP Amoxapine RS is used only for peak identification purposes.

Response: Comment incorporated.

Monograph/Section(s): Methotrexate/Multiple Sections

Expert Committee: Monographs—Small Molecules 3

No. of Commenters: 3

Comment Summary #1: The commenter suggested using the name “methotrexate related compound E free acid” for the impurity eluting at the relative retention time of 1.39, and including its complete chemical name as a footnote under the *Impurity Table 1*.

Response: Comment incorporated.

Comment Summary #2: The commenter suggested revising the designations for USP Methotrexate Related compounds H and I, to make them consistent with the designations of Impurities H and I in the *European Pharmacopoeia*.

Response: Comment incorporated.

Comment Summary #3: Commenter suggested replacing dimethyl sulfoxide which is used as a diluent under *Assay* and *Organic impurities* with the diluent specified in the European Pharmacopoeia monograph.

Response: Comment not incorporated because dimethyl sulfoxide is needed to ensure a complete dissolution of all known and unknown impurities.

Expert Committee-initiated Change: The third chemical name, based on the IUPAC nomenclature, is added to the Chemical Information section.

Monograph/Section(s): Polyglyceryl 3 Diisostearate/Content of Fatty Acids

Expert Committee(s): Monographs—Excipients

No. of Commenters: 1

Comment Summary #1: The commenter suggested that relative standard derivation: NMT 6.0 for the peak responses for palmitate and stearate should be decreased and a measure of repeatability of the area percent should be used.

Response: Comments not incorporated due to a lack of supporting data.

Monograph/Section(s): Powdered Bacopa Extract

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Label identification test B with the heading “HPLC Identification Test.”

Expert Committee-initiated Change #2: Replace the development distance in the TLC identification from about 90% to about three-fourths of the plate.

Expert Committee-initiated Change #3: Correct the particle size of the HPLC column stationary phase to 5 µm.

Monographs: Powdered Centella Asiatica Extract and Centella Asiatica
Triterpenes

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Label identification test B with the heading “HPLC Identification Test.”

Expert Committee-initiated Change #2: Replace the development distance in the TLC identification from about 90% to about three-fourths of the plate.

Monograph/Section(s): Powdered Garcinia Hydroxycitrate Extract

Expert Committee(s): Monographs—Dietary Supplements

Expert Committee-initiated Change #1: Label identification test A with the heading “HPLC Identification Test.”

Monograph/Section: Racemethionine/ Organic Impurities

Expert Committee(s): Monograph-Excipient Monograph

Expert Committee-initiated Change: The Expert Committee revised the Samples subsection in the Analysis section to the Organic Impurities, Procedure-Related Substances test to clearly state the correct nomenclature of the standards and samples utilized for the test.

Monograph/Sections: Schizochytrium Oil/Multiple Sections

Expert Committee: Monographs—Dietary Supplements

No. of Commenters: 2

Comment Summary #1: The commenter requested changing the *Title* from *Schizochytrium Oil* to DHA Algal Oil (*Schizochytrium* sp.).

Response: Comment not incorporated. The Expert Committee agrees with the previous (2005-2010) DS Expert committee’s decision to keep the *Title* as is. The Committee finds the use of acronyms and parenthesis not appropriate for a pharmacopeial title.

Comment Summary #2: The commenter requested changing DHA Content expression under the *Definition* from % (w/w) to mg/g.

Response: Comment not incorporated. In order to match the current industry practice, the labeling section in the monograph requires the article to be labeled in mg/g. The Expert Committee believes the DHA content in the *Definition* should be expressed in % (w/w) to match requirements from regulatory agencies and to maintain consistency with other USP monographs.

Comment Summary #3: The commenter requested removing *Fatty Acid Profile* test under the *Identification* because it is unnecessarily prescriptive and restrictive to define a safe and suitable product. Instead, the commenter suggested the incorporation of the following under the *Identification*: “DHA Algal Oil (*Schizochytrium* sp.) is characterized by significant amounts of long-chain C22 fatty acids. The sum of the area peak for DHA methyl esters is not less than 30%.”

Response: Comment not incorporated. The Expert Committee believes the *Fatty Acid profile* test is not unnecessarily prescriptive because the analytical procedure is already carried out for the assay. It is not unnecessarily restrictive because the fatty acid profile is a tool to characterize the oil source. In this case it allows differentiation from the two currently available algal sources of oils rich in DHA, and from enriched fish sources, which would become undistinguishable if the comment were adopted.

Comment Summary #4: The commenter suggested: (1) Changing the *Fatty Acid Profile* under the *Identification* to *Long Chain Unsaturated Fatty Acid Profile*, (2) Adding a formula for calculation the percentage of individual fatty acids to *Fatty Acid Profile*, and (3) Adding the relative retention times for the targeted fatty acids to the *Table* for *Fatty Acid Profile*.

Response: Comment incorporated.

Comment Summary #5: The commenter requested changing unit for the limit of inorganic impurities under the *Inorganic Impurities* from µg/g to mg/kg.

Response: Comment not incorporated. The Expert committee believes that the inorganic impurities limit should be expressed in µg/g to match the unit expression for this type of limits in other monographs in USP. The numerical value in µg/g is equivalent to the expression mg/kg and therefore the Expert Committee finds no reason to change it.

Comment Summary #6: The commenter requested changing the label of DHA content in the *Labeling* from mg/g to percentage (%).

Response: Comment not incorporated. The expression in percentage (w/w) is already in the definition to match the regulatory requirements. Therefore, the Expert Committee believes that labeling for the DHA content should be in mg/g to match the industry practice.

Monograph/Section(s): Schizochytrium Oil Capsules

Expert Committee: Monographs—Dietary Supplements

Expert Committee-initiated Changes: All the changes to the monograph were made in agreement with the changes proposed/approved for the dietary ingredient monograph. (See comments for Schizochytrium Oil).

The sections Strength, and Content of DHA were modified for consistency with the acceptance criteria in the Definition.

Response: Comments incorporated.

Monograph/ Section(s): Trandolapril Tablets/Organic Impurities

Expert Committee: Monographs—Small Molecules 2

No. of Commenters: 3

Comment Summary #1: The commenter requested widening the limits of impurities as follows: trandolaprilate - from NMT 0.5% to NMT 2.0%; trandolapril related compound D - from NMT 3.0% to NMT 5.0%; any other individual impurity - from NMT 0.2% to NMT 1.0%; and total impurities - from NMT 4.5% to NMT 7.0%. The widened impurity limits reflect the commenter's FDA-approved specifications.

Response: Comment incorporated.

Comment Summary #2: The commenters requested deleting the specification for trandolapril related compound C because it is a process impurity which is controlled in the drug substance monograph.

Response: Comment incorporated.

Monograph/Section(s): Trospium Chloride/Multiple Sections

Expert Committee: Monographs - Small Molecules 3

No. of Commenters: 4

Comment Summary #1: The commenter indicated that the chemical name listed in the chemical information section is using a naming convention which could be misleading, and requested the Expert Committee to revise it.

Response: Comment incorporated as follows: The chemical name is modified by replacing the (1 α ,3 α ,5 α) descriptors with (1R,3r,5S) descriptors which are based on the IUPAC nomenclature.

Comment Summary #2: Commenter reported difficulties in detecting Trospium Related Compound C at the 0.1% level.

Response: Comment not incorporated. The validation data from the sponsor and the results of USP collaborative testing do not support this observation.

Comment Summary #3: The commenter requested adding a test for *Appearance of solution*, to be consistent with the European Pharmacopoeia monograph.

Response: Comment not incorporated. Based on the information received from the sponsor, this test does not control any important quality attributes and will not add any value to the public standard. In addition, this test typically is not included in USP monographs as it is based on sensory perception and may be subjective.

Comment Summary #4: The commenter requested correcting the chemical name for Trospium Chloride Related Compound C by adding the missing word "chloride" which was inadvertently omitted from the proposal.

Response: Comment incorporated.

Monograph/Section(s): Zaleplon/Multiple Sections

Expert Committee: Monographs - Small Molecules 4

No. of Commenters: 3

Comment Summary #1: The commenter requested the limit for *Residue on Ignition* be increased from NMT 0.1% to NMT 0.2% to reflect the commenter's FDA-approved specifications.

Response: Comment incorporated.

Comment Summary #2: The commenter indicated that the proposed monograph does not monitor some of the process impurities observed in their product.

Response: Comment not incorporated. The Expert Committee is willing to consider future changes to the monograph upon the receipt of the necessary supporting data.

Comment Summary #3: The commenter requested revising the solubility information from "sparingly soluble in propylene glycol" to "slightly soluble in propylene glycol."

Response: Comment incorporated.

Monograph/Section(s): Zaleplon Capsules/Multiple Sections

Expert Committee: Monographs - Small Molecules 4

No. of Commenters: 3

Comment Summary #1: The commenter indicated that the *Sample solution* under *Identification by UV*, if prepared from the whole capsules, may result in the interference from the capsule shell components, and requested revising the *Sample solution* to indicate that it should be prepared from the contents of the capsules rather than the whole capsules.

Response: Comment incorporated.

Comment Summary #2: Two commenters requested widening the limit for any individual unspecified impurity from NMT 0.1% to NMT 0.2%, and the limit for total impurities from NMT 0.2% to NMT 1.0%, to reflect the commenters' FDA-approved specifications.

Response: Comment incorporated.

Comment Summary #3: The commenter requested revising the Dissolution test to add an option of quantifying the amount of zaleplon dissolved by HPLC procedure.

Response: Comment incorporated.

Comment Summary #4: The commenter requested inclusion of the Dissolution test for their FDA-approved product.

Response: Comment incorporated.