Pharmacopeial Discussion Group Meeting

Meeting Highlights

November 3-4, 2015
USP Headquarters
Rockville, Maryland, USA

1. Harmonization Topics Signed-off

1.1. General Chapters

1.1.1. Revised

Q-03/04 Uniformity of Content/Mass (USP)

This revision brings clarification of “Others” in Table 1: Dosage forms not addressed by the other categories in this table including but not limited to suppositories, transdermal systems (patches) and semisolid preparations applied cutaneously and intended for systemic distribution of the drug substance.

1.2. Excipients

1.2.1. Corrected – Addition or revision of a local requirement

1.2.1.1. E-32 Povidone (JP)

A revision to the cover sheet was made to address individual local requirements.

1.2.1.2. E-43 Wheat Starch, Rev. 2 (EP)

A revision to the cover sheet was made due to local requirement for JP: Total protein (Catalyst – TiO_2 instead of Se).

1.2.1.3. E-56 Glucose monohydrate/anhydrous (EP)

A revision to the cover sheet was made to replace the Identification (colour reaction) with Identification (IR-spectrophotometry) under USP local requirements.

1.2.1.4. E-64 Isomalt (EP)

A revision to the cover sheet was made due to local requirement for JP: the modified procedure uses a lower amount of Isomalt CRS

and to address Stakeholder concerns. PDG will verify supporting data necessary for the procedure in future revision.

2. Major Harmonization Topics

2.1.1. Viscosity of Cellulosics

2.1.1.1. E-08 Carmellose Sodium

The coordinating pharmacopeia provided a Stage 3 ver.3 proposal update on the viscosity test using Carmellose sodium. The concept of liaising the type of viscometer apparatus, spindle, speed, and concentration of the solution to the labelling was discussed.

2.1.2. ICH Q3D: Guideline for Elemental Impurities

Each pharmacopeia exchanged their updates and progress on the implementation of the ICH Q3D Elemental Impurities Guideline for their respective regions.

3. Harmonization Progress on PDG Work Programme

3.1. Topics undergoing harmonization

3.1.1. Q-03/04 Uniformity of Content (USP)

The coordinating pharmacopeia reviewed the *Stimuli* article: Stimuli to the Revision Process: An Evaluation of the Indifference Zone of the USP <905> Content Uniformity Test recently published. The article recommends keeping the current test and not pursuing a formal proposal for revision. Expert comments from PDG will be sent to the coordinating pharmacopeia.

3.1.2. G-07 Metal Impurities (USP)

The coordinating pharmacopeia sent a Stage 3 draft for review. Based on the number and scope of the comments received, PDG agreed to schedule an Expert teleconference meeting between the pharmacopeias to address comments.

3.1.3. G-08 Inhalation (EP)

PDG provided updates on the chapter. The coordinating pharmacopeia will organize a teleconference with PDG experts to discuss this chapter.

3.1.4. G-17 Uniformity of Delivered Dose of Inhalations (EP)

The coordinating pharmacopeia requested comments for the Stage 2 version 2 draft sent to PDG. PDG will review the draft and send comments to the coordinating pharmacopeia.

3.1.5. G-20 Chromatography (EP)

The coordinating pharmacopeia discussed the revised draft version of the chapter and will consider comments from PDG, including for system suitability requirements and modifications of chromatographic conditions especially for adjustments of column dimensions. The comments received will be further discussed with the Experts of the coordinating pharmacopeia.

3.1.6. G-21 Dynamic Light Scattering (JP)

The coordinating pharmacopeia addressed the comments from the Stage 2 draft and sent a Stage 3 draft proposal to PDG. PDG will review the proposal and send comments to the coordinating pharmacopeia.

3.1.7. B-04 Protein Determination (USP)

The coordinating pharmacopeia presented the USP chapter <507> text as an alternative to the Stage 4 proposal for total protein determination. PDG will consider the proposal and send feedback to the coordinating pharmacopeia.

3.1.8. B-05 Peptide Mapping (USP)

The coordinating pharmacopeia is preparing a revision and will setup a teleconference with PDG Experts once finalized.

3.1.9. E-04 Calcium Disodium Edetate (JP)

The coordinating pharmacopeia provided an update and PDG agreed to proceed with a Stage 4 draft.

3.1.10. E-06 Calcium Phosphate Dibasic Anhydrous (JP)

PDG discussed the Assay results and the proposal for changing the acceptance criteria. PDG agreed that further discussions are needed.

3.1.11. E-08 Carmellose Sodium (USP)

PDG reviewed the Stage 3, version 3 draft and discussed issues with the identification test by IR-spectrophotometry and the Assay test for degree of substitution (DS). More discussion with the Experts is needed. This monograph is one of two monographs in the pilot study for developing a harmonized procedure for viscosity.

3.1.12. E-17/E-18 Ethylcellulose (EP)/Hydroxyethylcellulose (EP)

Following discussion from the last meeting on the status on the harmonization activities of EC and HEC, PDG considered additional data provided by an individual Stakeholder.

For EC, the coordinating pharmacopeia presented and reviewed the data comparing the PDG proposed Assay method with individual Stakeholder method. The recommendation was to continue with the PDG proposed Assay method, although additional discussion with the Experts is needed. PDG is proposing to reach consensus by Mid-February 2016 in its path forward.

For HEC, the coordinating pharmacopeia presented the data comparing the PDG proposed Assay method with other Stakeholder method. In addition, an IR-spectrophotometric procedure for identification will be reviewed with Experts before moving forward.

3.1.13. E-23/E-24 Lactose anhydrous (USP)/Lactose monohydrate (USP)

An individual pharmacopeia reviewed two methods developed for Assay and Impurities. The other two pharmacopeias will review the results and respond to the coordinating pharmacopeia.

3.1.14. E-28/E-29 Petrolatum (USP)/Petrolatum, White (USP)

The coordinating pharmacopoeia presented lab data on the two methods for Polyaromatic Hydrocarbons (PAH) for determining an appropriate specification for PAH. A teleconference is scheduled with a Stakeholder organization for discussion on the method. Additional lab studies may be performed and the coordinating pharmacopeia will update PDG on the progress. The other two pharmacopeias will review the results and respond to the coordinating pharmacopeia. As part of the proposed method, PDG considered removal of the drop point method and replacing with the melting point method.

3.1.15. E-30 Polyethylene Glycol (USP)

The coordinating pharmacopeia is working to develop a test for formaldehyde and acetaldehyde which is based on the method in PEG 3350 in USP. The coordinating pharmacopeia presented lab results on various grades of PEG using different sample conditions for the method. The other two pharmacopeias will review the results and respond to the coordinating pharmacopeia.

3.1.16. E-32/E-54 Povidone (JP)/Copovidone (JP)

PDG shared results on method development on a new GPC method under consideration for replacement of the nonspecific Nitrogen Kjeldahl Assay method, as well as to detect for possible adulterants and impurities. Method development is on-going and the method will be shared with PDG once complete.

3.1.17. E-33/E-34/E-35 Saccharin/Saccharin Sodium/Saccharin Calcium (USP)

The coordinating pharmacopeia provided an update on Assay lab results from different manufacturing processes. The coordinating pharmacopeia will proceed with method validation and submit a report to PDG for feedback.

3.1.18. E-36/E-37 Silicon Dioxide (JP)/Silicon Dioxide, Colloidal (JP)

The coordinating pharmacopeia discussed the progress on development of a suitable identification test. The Trade association, IPEC, is in the process of conducting a collaborative round robin study and preparing a protocol. PDG will review results when IPEC completes the study.

3.1.19. E-43 Wheat Starch (EP)

The coordinating pharmacopeia reviewed the comments on the test for total protein and provided answers to the other pharmacopeia's questions that will be further considered by PDG.

3.1.20. E-44 Stearic Acid (EP) – Discussion on inclusion of JP alternative apparatus in the harmonized test for freezing point

PDG discussed inclusion of JP alternative apparatus in harmonized test. The individual pharmacopeia will send a protocol by the end of December and samples for testing by the end of January.

3.1.21. E-46 Talc (USP)

The coordinating pharmacopeia provided an update on revising the current asbestos testing for Talc and is currently recruiting Talc Methods experts to form an Expert Panel.

3.1.22. E-51 Glycerin (USP)

The coordinating pharmacopeia provided updates on strengthening the GC assay method and currently setting an appropriate Assay specification limit. In addition, two methods are being considered for the Aldehydes method.

3.1.23. E-53 Calcium Carbonate (JP)

The coordinating pharmacopeia provided an update on the Identification tests and application of the Q3D guideline for elemental impurities. The individual pharmacopeia will review these comments with its Experts.

3.1.24. E-61 Starch, Pregelatinized (JP)

The coordinating pharmacopeia provided preliminary data results from an IPEC-Japan study to discriminate between pregelatinized starch and partially pregelatinized starch by viscosity testing. The coordinating pharmacopeia will report results from the first step of the study by the end of December and proposed a collaborative round robin study with the IPEC Federation.

3.1.25. E-62 SWFI in Containers (USP)

The coordinating pharmacopeia reviewed the meeting notes of the SWFI Expert Meeting in July on reviewing SWFI specifications in PDG and will complete actions from the meeting once all comments are received.

3.1.26. E-63 Lactose for Inhalation (USP)

The coordinating pharmacopeia discussed earlier the assay/impurities under Lactose anhydrous/monohydrate. The coordinating pharmacopeia will determine how PDG members handle critical material attributes for inhalation grades.

3.2. Revision Proposals

3.2.1. Q-09 Particulate contamination (USP)

The coordinating pharmacopeia reviewed the revision proposal for the harmonized chapter and will review comments received from PDG.

3.2.2. E-10 Microcrystalline Cellulose (USP)

The coordinating pharmacopeia reviewed comments on the proposed revision updates for the identification test by IR-spectrophotometry. Continued discussion is planned.

3.2.3. E-60 Sodium Lauryl Sulfate (USP)

The coordinating pharmacopeia reviewed the revision proposal, which had issues with determining the endpoint in the assay by volumetric titration. The results from the modified method using a different indicator were reviewed.

4. Discussion of PDG Process

4.1. Improvement of Working Procedure

PDG discussed an alternative model to determine Stage 6C Indication of Harmonization in order to streamline the process, and improve transparency to our stakeholders through a formal acceptance at Stage 6C. PDG agreed to consider a few examples for the next PDG meeting to determine feasibility.

5. Correction

Topic 3.1.13 was corrected to E-32 Povidone (JP) and E-54 Co-Povidone (JP) from the Meeting Highlights of the June 30-July 1, 2015 PDG Meeting in Tokyo, Japan.

6. Next Meeting

The next meeting will take place May 25-26, 2016 in Strasbourg, France.