Pharmacopoeial Discussion Group Meeting
30 June-1 July 2015

Meeting Highlights

PMDA office
Shin-Kasumigaseki Building, 3-3-2 Kasumigaseki, Chiyoda-ku,
Tokyo, JAPAN

1. Harmonisation Topics Signed-off

1.1. Excipients

1.1.1. Revised

1.1.1.1. E-32 Povidone Rev. 1(JP)

The revision was requested on conditions regarding testing for the impurity monomers. Through discussion on the revision, other specifications were reviewed also and in the sign-off text:

- IR test is moved to the harmonised attribute;
- Testing for the impurity monomers (1-vinyl-2-pyrrolidone and 2-pyrrolidone) is refined in terms of testing conditions;
- Formic acid test incorporates system suitability;
- Aldehydes testing is editorially corrected; and
- In reagents section, the “acetaldehyde ammonia trimer trihydrate” incorporates titration.

1.1.2. Corrected

1.1.2.1. E-44 Stearic acid (The revision of sign-off cover page) (EP)

An alternative apparatus for testing freezing point was introduced as JP local requirement. PDG will verify supporting data necessary for including the apparatus in harmonised text in future revision.

1.1.2.2. E-20 Hydroxypropylcellulose low substituted, Corr.1 (USP)

Maximum permitted weight loss was converted from percentage to milligrams.

1.1.2.3. E-21 Hypromellose, Rev. 1, Corr.1 (JP)

The temperature conditions for the viscosity method were added.

1.1.2.4. E-26 Methylcellulose, Rev. 2 Corr.1 (JP)

The temperature conditions for the viscosity method were added.

2. Major Harmonisation Topics

2.1. Viscosity tests: USP report on progress (USP)

The coordinating pharmacopoeia provided an update on the viscosity test currently used in the three monographs which are subject of a pilot project:

For Carboxymethylcellulose (CMC) Sodium and Hydroxyethylcellulose (HEC), the specifications are being developed in collaboration with manufacturers;

For Low Substituted Hydroxypropylcellulose (L-HPC), after further discussions, the monograph is removed from this pilot project.

2.2. Other topics

2.2.1. ICH Q3D implementation in each pharmacopoeia and relevant information exchange.

The three pharmacopoeias exchanged information on their respective approaches for the implementation of ICH Q3D guideline. In addition, PDG confirmed commitment to harmonise the general chapter on testing procedures for elemental impurities.

3. Harmonisation Progress on PDG Work Programme

3.1. Topics undergoing harmonisation

3.1.1. G-07 Metal Impurities (USP)

The coordinating pharmacopoeia presented a Stage 3 draft to PDG for comment in preparation for presenting a Stage 4 draft for public inquiry.

3.1.2. G-20 Chromatography (EP)

As a follow-up from recent PDG decisions on PDG process improvement, a teleconference with experts from the 3 regions had taken place in May allowing significant progress to be made in the resolution of major sticking points. The coordinating pharmacopoeia will work on the resolution of a number of other items with the aim of finalising a Stage 4 draft for public inquiry for the next PDG meeting.

3.1.3. G-21 Dynamic Light Scattering (JP)

PDG identified the need for a teleconference with experts to discuss the best way to collect feed-back on the technique and on the utility of such a chapter.

3.1.4. B-04 Protein Determination, Rev. 1 (USP)

PDG decided to put the publication of the Stage 4 text on hold until the coordinating pharmacopoeia has shared an alternative draft containing additional system suitability criteria for each methodology described. After the other pharmacopoeias have reviewed this draft, a decision will be made as to which text is suitable for all regions to publish as a Stage 4 proposal. The finalisation of the Stage 4 draft for public inquiry is aimed for the next PDG meeting. The coordinating pharmacopoeia will consider organising a teleconference.

3.1.5. B-05 Peptide Mapping, Rev. 1 (USP)

The coordinating pharmacopoeia will review the comments raised in the other regions which principally refer to the expansion of the parts related to system suitability and the setting up of acceptance criteria. A teleconference with experts from the 3 regions to address these issues will be organised by the coordinating pharmacopoeia this autumn.

3.1.6. E-08 Carmellose Sodium (USP)

The coordinating pharmacopoeia is finalising a Stage 3 draft for PDG comment in preparation for presenting a Stage 4 draft for public inquiry.

3.1.7. E-17 Ethylcellulose, Rev. 2 (EP) and E-18 Hydroxyethylcellulose (EP)

Following the PDG/IPEC meeting in November 2014, IPEC had agreed to supply data and explanations concerning differing assay results to PDG. However, IPEC informed PDG in a letter in May 2015 that they did not plan to conduct further testing on those methods but would share their in-house methods with PDG. In the absence of any further information PDG decided to postpone the final decision whether to continue the harmonisation of these monographs or not to the next meeting in Rockville in November 2015.

3.1.8. E-28 Petrolatum (USP) and E-29 Petrolatum, White (USP)

The coordinating pharmacopoeia is evaluating two methods for Polyaromatic Hydrocarbons (PAH), in order to determine an appropriate specification for PAH.

In addition to evaluation of PAH, PDG decided to work on the resolution of other issues such as drop point with the aim of finalising the harmonised text as early as possible.

3.1.9. E-30 Polyethylene Glycol (USP)

The coordinating pharmacopoeia is working to develop a test for formaldehyde and acetaldehyde which is based off of the method in PEG 3350. The coordinating pharmacopoeia is working on evaluating different sample conditions for the method to be representative of the various grades of PEG on the market.

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

The coordinating pharmacopoeia appreciates the inputs from the IPEC federation member including the results from evaluation of the identification method for infrared absorption spectrum that distinguishes between the two grades. PDG will continue collaborating with IPEC and review the results of IPEC's round-robin testing among relevant suppliers in the three regions.

3.1.11. E-43 Wheat Starch, Rev. 3 (EP)

The coordinating pharmacopoeia provided the study results for total protein. The other two pharmacopoeias will review the results by the next PDG meeting.

3.1.12. E-46 Talc potential revision, (USP)

The coordinating pharmacopoeia received comments from the other two pharmacopoeias on a proposal presented to ensure that the tests contained in the Absence of Asbestos section have adequate specificity. The coordinating pharmacopoeia will send a formal response to these comments to PDG and will develop the specific methods to be proposed to PDG.

3.1.13. E-32 Povidone (JP) and E-54 Copovidone (JP)

PDG shared technical considerations including those on a new GPC method which preliminary data suggests may be able to serve as an alternative to the Kjeldahl Assay method, as well as detect for possible adulterants and impurities. This work is in response to concerns with intentional adulteration with nitrogen-containing substances.

3.1.14. E-54 Copovidone (JP)

The coordinating pharmacopoeia will send out a draft for public consultation in July for the three pharmacopoeias to publish according to their respective schedules.

3.1.15. E-61 Starch, Pregelatinised (JP)

The coordinating pharmacopoeia briefly introduced results of preliminary consideration of another apparatus and noted the necessity to include the degree of pregelatinisation as part of the Identity. The coordinating pharmacopoeia will solicit input from stakeholders and share them in the next meeting.

3.1.16. E-62 SWFI in Containers (USP)

The coordinating pharmacopoeia will organise a technical teleconference in July for the purpose of experts to discuss sticking points. The coordinating pharmacopoeia will consult relevant experts on the current proposal for replacing the existing oxidisable substances test with total organic carbon (TOC).

3.2. Revision Proposals

3.2.1. Q-06 Bacterial Endotoxins (JP)

Following requests from users to include recombinant factor C reagent as an alternative to the animal-sourced Limulus Amoebocyte Lysate (LAL) reagent in the general chapter on bacterial endotoxins, PDG decided not to revise the chapter at this stage and limit its use strictly to LAL.

4. Discussion of PDG Process

4.1. PDG Process Improvement

4.1.1. PDG Website

PDG agreed to update the “implementation time table” and the “state of works” simultaneously with preparation of the Press Release and the Meeting Highlights.

4.1.2. Improving working procedures

In order to further stream-line their activities, PDG agreed to prioritise in the future harmonisation of general chapters. In addition, to ensure expediting progress, both target date for initiating public consultation (Stage 4) and sign-off will be defined for all topics relating to general chapters currently on the work-program.

4.2. Transparency for the sister pharmacopoeias

In order to provide increased transparency on its activities, PDG will offer an easy way to access information on its work program to its sister pharmacopoeias, including the possibility to provide comments on draft texts during the consultation period. Respective information will be shared at the next WHO international meeting of World Pharmacopoeias.

5. Date of the next meeting – to be hosted by USP

The next meeting is proposed for 3-4 November 2015 in Rockville, Maryland, USA.