Pharmacopoeial Discussion Group Meeting

Meeting Highlights

18-21 October 2022
Videoconference
Hosted by the Japanese Pharmacopoeia

1. Future of the PDG

The PDG has been working on three areas considered as key to ensuring the future of the Group.

1.1. Pilot phase for opening up to other pharmacopoeias

At the annual meeting on 5-8 October, 2021 (link), the PDG decided to launch a pilot phase to integrate additional pharmacopoeias from regions not yet represented in the PDG. After a detailed review of each application, as reported in the press release in the September 2022 (link), the PDG agreed by consensus to welcome the Indian Pharmacopoeia Commission (IPC) as a pilot participant. As it was the first time the IPC had taken part in a PDG meeting, the IPC introduced its organisational structure, its pharmacopoeia and its plan for harmonising its texts with the PDG workplan. The established PDG members and WHO presented an outline of the activities of the PDG and of each pharmacopoeia, to provide an insight into PDG and processes. The IPC would join all applicable PDG activities for this one-year pilot phase beginning at this annual meeting in 2022, and the established PDG members would evaluate the outcome of this pilot at the next annual meeting in 2023.

1.2. Stakeholder engagement

The PDG had discussed how to get stakeholders involved at earliest stages of the harmonisation process. A draft concept paper for the early engagement model for stakeholders was proposed using the excipient “Polysorbate 20” as a pilot; this was accompanied by a revision proposal for the existing PDG monograph, “Polysorbate 80” which contained methods similar to those of “Polysorbate 20”. The PDG would discuss how to involve stakeholders on the proposals included in the concept paper after an in-depth review by the PDG pharmacopoeias.

1.3. Regulatory engagement

The PDG had also discussed how to improve the engagement of regulators. As a first step in these activities, the EP, the JP and the USP reported on the interactions with their respective regulators and exchanged their opinions. As an example for the other members and to deepen their understanding of regulations in Japan, the JP (as the host of the meeting) gave a detailed explanation of the interactions with its own regulators (i.e. the Ministry of Health, Labour and

Welfare: MHLW and the Pharmaceuticals and Medical Devices Agencies: PMDA) on adoption of the ICH Q3D guideline. The PDG members agreed to continue the open dialogue to further their understanding of the challenges to pharmacopoeial harmonisation arising from their different regulatory environments.

2. ICH Q4B maintenance

As the host of the PDG meeting, the JP summarised the discussions and the outcomes of the recent proof-of-concept study for the maintenance of the ICH Q4B annexes (link). Following the discussion at the PDG interim videoconferences on 15 and 28 March 2022 (link), draft revisions of three selected Q4B annexes (Annex 6: Uniformity of Dosage Units, Annex 7: Dissolution and Annex 8: Sterility) had been prepared. Based on these drafts, the PDG prepared and summarised reports with recommendations for some key questions that had been raised in this proof-of-concept study. The PDG reported the conclusions of this study with recommendations for next steps to the ICH Assembly in November 2022.

3. Harmonisation Topics Signed off

Owing to the COVID-19 pandemic, individual work programme sign-offs would be handled by correspondence after the 2022 annual meeting. As ever committed to transparency, the PDG would publish the full texts signed off in 2022 on each pharmacopoeia's website (links: general chapters, general methods, biotechnology, monographs)

3.1. General Chapter

3.1.1. New

3.1.1.1. G-21 Particle Size Analysis by Dynamic Light Scattering (JP)

The PDG signed-off this new text. This chapter could be used to determine the average hydrodynamic particle size and the broadness of the size distribution of submicron particles dispersed in a liquid. Particle size distribution is an important characteristic of dispersed systems such as emulsions, suspensions and liposomal formulations.

3.1.2. Revised

3.1.2.1. G-02 Bulk Density and Tapped Density (EP)

The PDG agreed to sign off this text, which had been revised to change the definition of "bulk density" to be the ratio of the mass of a powder sample to its volume, independently of how it is packed. "Untapped bulk density" and "tapped bulk density" are now used as subcategories. Accordingly, the chapter title was revised to change from "Bulk Density and Tapped density of Powders" to "Bulk Density of Powders".

3.1.2.2. G-05 Powder Flow (EP)

The PDG agreed to sign off this text. In addition to the change of terms to align with G-02 Bulk Density and Tapped Density, the Flow Through an Orifice and the Shear Cell Methods sections were updated.

3.1.2.3. B-05 Peptide Mapping (USP)

The PDG agreed to sign off this text. This was a general revision to take into account recent developments and current practices including modernisation of the equipment and methods used. The text now

described the major steps in developing a peptide mapping procedure in dedicated sections and a flow diagram had been introduced to outline the steps and decisions when developing a peptide mapping procedure.

3.2. Excipients

3.2.1. Corrected

3.2.1.1. E-07 Carmellose Calcium (USP)

The PDG agreed to sign off the correction of this text to specify the sample amount for the Loss on Drying, add a note on the reagents used in the Limit of Sulfate test and to add the section on Labelling as a harmonised attribute.

3.2.1.2. E-20 Hydroxypropylcellulose, Low Substituted (EP)

3.2.1.3. E-21 Hypromellose (EP)

3.2.1.4. E-26 Methylcellulose (EP)

The PDG agreed to sign off these texts, which had been corrected to remove the exact size specifications for reaction vials and the heating block used in the Assay test while focussing on the important aspect of the volume of the vial and its air-tightness.

3.2.1.5. E-23 Lactose, Anhydrous (EP)

3.2.1.6. E-24 Lactose, Monohydrate (EP)

The PDG agreed to sign off the corrections of these texts to remove the TLC test from the harmonised text due to the differences in the status of the test in the EP and the USP. While the USP required the test in addition to an IR identification, the EP prescribed it as part of an alternative test series that may only be used in pharmacies. The EP and the USP would keep the test unchanged as their local requirements.

3.2.2. Correction of sign-off cover sheet

3.2.2.1. Deletion of heavy metals and individual impurity tests (JP)

It was agreed to correct the sign-off coversheets for 30 excipients to reflect the revision of these monographs in the JP18-1 in response to JP's implementation of the ICH Q3D guideline.

3.3. Other texts

3.3.1. PDG Confidentiality Commitment

The PDG drafted a PDG specific Confidentiality Commitment to emphasise in writing that the information required to support the PDG's efforts to harmonise excipient monographs and general chapters would be handled confidentially by all involved parties. The commitments had been signed by each participating pharmacopoeia.

4. PDG Work Programme

4.1. Discussion/Decision on way forward for topics requiring specific emphasis

4.1.1. General Chapters

4.1.1.1. G-07 Elemental Impurities (USP)

The co-ordinating pharmacopoeia updated the PDG on the status of

this item and the next steps to complete the initial harmonisation were discussed. The key remaining question was focused on the validation requirements. PDG would continue discussions with the aim of harmonising this item in the near future.

4.1.1.2. G-20 Chromatography (USP)

The USP provided a detailed explanation of its plan to delay the implementation of the requirements for System sensitivity and Peak symmetry as specified in G-20 chromatography in light of stakeholder comments received. The EP and the JP shared with the USP their implementation approaches that had not led to a similar situation. The USP would move forward with the delay implementation of these two requirements.

4.1.2. Excipients

4.1.2.1. E-46 Talc (EP)

The EP shared an update on the status of asbestos testing in the EP general chapter that was under consideration for inclusion in the harmonisation work on E-46 Talc.

5. Any Other Business

5.1. Improving the Pharma Environmental Footprint: USP Initiative

The USP shared with the PDG its efforts to create more sustainable test methods through modernization, such as by reducing the use of toxic / hazardous solvents and reagents. The USP asked if or how PDG would also like to explore ways to improve sustainability through efficiencies with global harmonisation. Through global harmonisation of test methods, repetitive testing could be avoided and this would also help reduce the environmental footprint of medicinal products. Opportunities were discussed, with the USP to come back to the PDG with further thoughts at the next meeting.

6. PDG Work programme

As announced in the 2021 Annual Meeting Highlights (link), the PDG has considered adding further important items to its work programme while focusing on moving forward all active items on its work programme and concentrating its efforts on the pilot phase for expansion. Following the discussion at the interim videoconference in March 2022 (link) and in view of all other ongoing efforts, the PDG was pleased to add three items “Polysorbate 20”, “Purified Water” and “Water for Injection” to its work programme in response to stakeholders’ request. The PDG would work towards harmonisation of these impactful excipients.

7. Next Meeting

The next annual meeting will be hosted by the USP, on 3-4 October, 2023 in Hyderabad, India.