Pharmacopoeial Discussion Group Meeting

Meeting Highlights

5, 6, 7, 8 October 2021
Videoconference
Hosted by the European Pharmacopoeia

1. **Future of the PDG – pilot phase for opening up to other pharmacopoeias**

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

   (1) membership expansion as a means of enhancing its global outreach,
   (2) stakeholder engagement and
   (3) regulatory engagement.

   As the first key decision reached after intensive discussions, the PDG agreed to launch a pilot phase to integrate additional pharmacopoeias from regions not yet represented in the PDG. This milestone decision marks a critical step in the PDG's commitment to expanding recognition of harmonised pharmacopoeial standards.

   The PDG adopted a framework for accession of new members that includes a pilot phase as well as entry criteria for new members. These criteria will help to ensure that the successes of pharmacopoeial harmonisation achieved over more than three decades will be maintained and that the PDG will continue to work effectively. One entry criterion would be that a PDG harmonised text is expected to be implemented by all participating pharmacopoeias. New members would therefore need to commit to apply all the PDG harmonised chapters and monographs relevant to their market within a reasonable timeframe, unless they are already considered as harmonised with the PDG texts.

   In the weeks after the meeting, the PDG invited other world pharmacopoeias that were not yet represented to join a one-year pilot phase starting from the PDG annual meeting in autumn 2022.

   Additional information can be found in the dedicated PDG press release on the topic (Link).

2. Harmonisation Topics Signed off

Owing to the COVID-19 pandemic, individual work programme sign-offs were handled by correspondence after the 2021 annual meeting. As ever committed to transparency, the PDG has published the full texts signed off in 2021 on each pharmacopoeia's website (link).

2.1. New General Chapter

2.1.1. G-20 Chromatography (EP)

The PDG signed off the new text *G-20 Chromatography*. This chapter describes core requirements applicable for TLC, HPLC and GC. Particular attention was paid to terminology definitions and interpretation of chromatograms, system suitability requirements, adjustment of chromatographic conditions and quantitation procedures (see press release "PDG signs-off on milestone harmonised general chapter on chromatography" here). These harmonised requirements promote the development of individual monographs with a consistent approach and they enhance the understanding of basic requirements by users in all three regions.

2.2. Corrected General Chapter

2.2.1. G-01 Analytical Sieving (JP)

The PDG agreed to sign off a correction of the general chapter *G-01 Analytical Sieving* to adapt the frame diameters for sieves to those specified by standards in the different regions, i.e. 200 mm and 203 mm (8 inch) as well as 75 mm and 76 mm (3 inch).

2.3. New Excipient Monographs

2.3.1. E-28 Petrolatum (USP)

2.3.2. E-29 Petrolatum white (USP)

The PDG signed off these two closely related new monographs. It is a great achievement for the PDG to have reached consensus and to have finalised the development of these two new harmonised standards for the three regions. With the support of stakeholders, an appropriate analytical procedure and a limit for polycyclic aromatic hydrocarbons (PAH) – which are toxic carcinogens – have been established. The harmonised test

method was developed based on comprehensive comparative studies and extensive sample testing. The PAH specification limits also accommodate regulatory requirements in the three regions.

2.4. Revised Excipient Monograph

2.4.1. E-44 Stearic acid (EP)

The PDG agreed to sign off this text which had been revised to add to the monograph text an alternative Freezing point apparatus complying with JP <2.42> Congealing Point Determination.

2.5. Other changes to Excipient Monographs

The PDG agreed to sign off corrections of two excipient monographs (E-11 Powdered Cellulose and E-22 Hypromellose Phthalate).

2.6. Statement of Harmonisation Policy and Working Procedure

The PDG agreed to sign off a general revision of the PDG Statement of Harmonisation Policy. The revised text takes into account current practices and has also been expanded to cover the maintenance of the ICH Q4B annexes, a task that was given to the PDG by the ICH in 2018.

The PDG also agreed to sign off a revision of the PDG Working Procedure. This revision includes an update to the revision process to better address urgent needs in one region for public health reasons and adds a new paragraph with explanations on the process for suppressing items from the work programme.

3. ICH Q4B guideline and annexes

As the host of the PDG meeting, the European Pharmacopoeia (Ph. Eur.) summarised the latest information on this project which is intended to achieve broader interchangeability between pharmacopoeial methods in different pharmacopoeias.

In November 2020, the ICH Assembly approved the proposal by the PDG on how to extend the scope of the Q4B process to pharmacopoeial texts of the non-Founding and non-Standing ICH Regulatory Members. The proposed “proof-of-concept” pilot study on three selected Q4B annexes (Annex 6: Uniformity of

Content/Mass, Annex 7: Dissolution Test and Annex 8: Sterility Test) was launched by the PDG at the beginning of 2021.

The PDG had received from four pharmacopoeias of the non-Founding ICH Regulatory Members an outcome of the evaluation of their own texts versus the PDG sign-off text.

The PDG had reviewed this feedback and concluded that additional information from some of these pharmacopoeias was needed and would be requested before being able to update the respective Q4B annexes.

The PDG had agreed to present a status update at the next ICH Assembly meeting (17 and 18 November 2021).

4. Update on PDG-IMWP Pilot on sharing draft and final PDG texts

The PDG had analysed the outcome of the pilot phase and decided that draft texts for comments during the public consultation phase and final sign-off texts before implementation would continue to be published on each pharmacopoeia's website and to be shared with other non-PDG pharmacopoeias on a regular basis. This way forward proves the commitment of the PDG to transparency towards its stakeholders.

Following the pilot phase, the PDG will inform other, non-PDG pharmacopoeias about any PDG publications (i.e. draft texts for public consultation and final sign-off texts) in order to improve and speed up communication. The PDG also continues to welcome comments from other pharmacopoeias. These will be analysed by the co-ordinating pharmacopoeia and discussed within the PDG.

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

5.1. General Chapters

5.1.1. Bacterial Endotoxin Test (BET) / recombinant Factor C (rFC) (EP)

The PDG reviewed the status of the corresponding texts in the three pharmacopoeias as well as a gap analysis of the different approaches of the pharmacopoeias that had been performed in recent months and which had been discussed in a technical teleconference. A further technical teleconference attended by experts from each pharmacopoeia will be organised not only to get a clearer picture of the commonalities and

differences, but also to look into opportunities for harmonisation of this analytical method. The final decision on the proposal to launch a revision of chapter Q-06 Bacterial endotoxins by one of the participating pharmacopoeias to include a new method G that uses recombinant factor C as reagent will be taken at the PDG March 2022 videoconference.

5.2. Excipients

5.2.1. E-23 Lactose, Anhydrous/ E-24 Lactose, Monohydrate (USP)

The co-ordinating pharmacopoeia updated the PDG on the status of these items and the next steps in the revision of both monographs were discussed. The discussions were focussed on the inclusion of tests for inhalation grades and the tests for Bacterial Endotoxins and Microbial Limits. The potential HPLC method for Assay and Related Substances was also discussed.

5.2.2. E-45 Sucrose (USP)

A revised monograph proposal had been published for public consultation with a new Assay and Impurity test using a HPLC-Refractive Index (HPLC-RI) analytical procedure. The co-ordinating pharmacopoeia gave an update on the status of this item and was still reviewing the comments received from stakeholders during public consultation and from the other two pharmacopoeias. Significant progress was made and discussions will continue around several open questions.

5.2.3. E-62 Sterile Water for Injections in Containers (USP)

The co-ordinating pharmacopoeia gave an update on this important item and presented the next steps. While other issues were addressed, the discussions focussed on updating the TOC test and limit. In-depth discussions on the data provided would be needed before further progress could be made on the topic.

6. PDG Work plan

The PDG is considering adding a few further important items to its work plan, but will focus on moving forward all active items on its work plan (elaboration and revisions of texts) and will concentrate its efforts on the pilot phase for expansion of the PDG.

7. Next Meeting

The next annual meeting will be hosted by the JP, either on 18 and 19 October 2022 in Tokyo, Japan or on 18 to 21 October 2022 by videoconference.