SUMMARY MINUTES

of the

BRITISH PHARMACOPOEIA COMMISSION

A meeting of the British Pharmacopoeia Commission was held via videoconference on Monday 5th July 2021.

Present: Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Dr E Amirak, Dr A Barnes, Dr J Beaman, Dr A M Brady, Dr G Cook, Dr A Gleadle (*lay member*), Dr V Jaitely, Mr R Lowe, Dr P Marshall, Professor J Miller, Professor M Simmonds, Dr R Torano and Dr P Varley.

In attendance: Mr J Pound (*Secretary & Scientific Director*), Dr F J Swanson.

An apology for absence was received from Ms S Palser (*lay member*).

Also present: Ms H Corns, Mr P Crowley, Mr L Elanganathan, Mr A Evans, Mr A Gibb, Mr G Kemp, Mr S Maddocks, Mr R Smith, Ms A Thomson, Mr M Whaley and Mr S Young.

460 **Introductory Remarks**

Welcome The Chair welcomed members to the meeting.

Declaration of Interests; Confidentiality of Proceedings Members were reminded of the need to inform the Secretariat of any changes to their interests throughout the year and of the need to declare any specific interests at the start of relevant discussions. The Chair reminded members of the confidential nature of the meeting and that the papers should not be disclosed.

BPC Appointments Professor Taylor's second term as Chair had been extended for one year until 30th September 2022.

BPC Appraisals The Chair thanked members for participating in the appraisals process which had been undertaken by correspondence.

I MINUTES

461 The minutes of the meeting held on 15th March 2021 were confirmed.

II MATTERS ARISING FROM THE MINUTES

462 The following matters arising from the meeting held on 15th March 2021 were noted.

Minute 422 – Expression of Related Substances Limits (*November 2020 meeting refers*) Numerical limits would start to be included in BP monographs from the BP 2023 onwards and members would start to see examples in their routine EAG work.

Minute 441 – Working Party ATMP: Progress Report The draft Guidance on the Application of Flow Cytometry for the Cell and Gene Therapy Community had been published on the BP website in April.

Minute 444 – BPCRS Principles, Availability and Strategy Discussions were ongoing within the Secretariat to ensure that a harmonised approach relating to BPCRS was presented at future EAG meetings.

Minute 448 – Analytical Methods Evaluation Assessment An updated version of the Laboratory Evaluation Risk Assessment process would be provided at a future meeting.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

463 Updates from the Secretary & Scientific Director

Mr Pound provided an update on how the BP and MHRA were responding to the global Coronavirus (COVID-19) outbreak and other key issues.

OPERATIONAL

464 Expert Advisory Group PCN: Pharmacy and Nomenclature COM(21)19

The first meeting of the new Expert Advisory Group PCN, formed by merging the existing Pharmacy and Nomenclature EAGs, had been held on 30th June. Professor Jeffrey Aronson (former Chair of EAG NOM) had taken on the role of Chair and Mr Robert Lowe had agreed to act as Vice-Chair. Dr Rodney Horder (former Chair of EAG PCY) had agreed to remain on the EAG in view of his continuing role as Chair of Ph Eur Group 12: Dosage Forms and Methods. The meeting had been very successful and had included several agenda items that would previously have been discussed separately by both EAG NOM and EAG PCY.

465 Monograph Titles: Formulated Preparations COM(21)20

Current BP Policy The current policy relating to monograph titles for BP formulated preparation monographs was that the shortest title combining the name of the active moiety and the appropriate standard term should be used. Where the active ingredient was in the form of a salt, this was usually omitted from the title unless the **same dosage form** was available containing more than one form of the same active substance, for example both base and salt forms. It was noted that BP monograph titles were referenced in the British National Formulary (BNF) and in the Dictionary of Medicines and Devices and were used by the MHRA as the basis for naming generic medicines.

Ph Eur Finished Product Monographs The European Pharmacopoeia Commission had agreed that separate monographs should be developed for finished products that contained different forms of the same active ingredient and that the title of each monograph should include the full name of the relevant active ingredient, whether as the base, acid or salt form.

Future BP Policy In light of the recently adopted Ph Eur policy, members were invited to discuss the approach for future BP monographs. It was agreed that the current policy for BP monographs should be retained and that approved synonyms should be created for future Ph Eur monographs reproduced in the BP (as required). This approach would cause the least confusion for users and the use of approved synonyms was already well-established for instances where the BP adopted a different title from the Ph Eur for an active substance monograph.

After further discussion it was agreed the situation should be kept under review as the number of Ph Eur product monographs increased.

466 **Code of Practice for Scientific Advisory Committees** COM(21)21

Introduction The working practices and governance of the BP Commission and the Secretariat had been examined against the current Code of Practice for Scientific Advisory Committees and taking note of the Rules Governing the Proceedings of the British Pharmacopoeia Commission. It was noted that the Code of Practice provided a general guidance framework relating to the establishment, management and conduct of the committees to which it applied. It was up to the relevant sponsoring organisations and committees to determine the best approach for their particular situation.

Review of current Guidance Members were provided with the findings from the review, which had demonstrated that the BPC operated in accordance with the guidance. The review highlighted the current position for the BPC and included some proposals for minor changes and improvements.

467 **BPC Lessons Learned Workshop: Outcomes** COM(21)22

A summary of the comments received during the lessons learned workshop held after the March meeting, together with comments provided by those members who were unable to attend in person, was provided for information. The consensus was that most aspects of the work relating to the BP Commission were operating well and several suggestions and recommendations for improvement had been made.

General points The points raised related to the usual BPC/EAG business and ways of working. Some issues were already being addressed such as providing additional information on the website, providing clarity around members' interests and introducing a regular review of monographs.

Information/Induction for New Members A number of suggestions had been made to help new members become familiar with the work of the BP Commission and these would be incorporated as part of the induction process for future new members.

468 **Declaration of Interests: Guidance** COM(21)23

Guidance At the last meeting it had been agreed that it would be helpful if further guidance could be provided relating to interests held by members of the BP Commission and the Expert Advisory Groups, Panels of Experts and Working Parties.

Additional information and guidance had been prepared together with some examples of types of interest that might be declared and recommendations for the approach to take during meetings.

Members welcomed the additional clarification and guidance provided and it was agreed that the list of examples would be helpful for both Chairs and members.

469 **AQbD Strategy Update** COM(21)24

The Commission was updated on recent Analytical Quality by Design (AQbD) activities relating to the three strategic areas identified in the MHRA AQbD strategy document.

Supporting and Enabling Innovation It was intended that further practical evaluations would be carried out and the Secretariat were planning a collaborative study using the Analytical Target Profile approach.

Collaboration, Engagement and Knowledge Transfer Stakeholders were keen to receive information on the application of AQbD for pharmaceutical analysis and the BP and MHRA continued to engage with interested parties and organisations to raise awareness and promote the exchange of information. Following the success of the joint BP/USP webinar held in February a further two-day event had been arranged for later in the year.

Application to Public Quality Standards The AQbD Working Party had initiated a joint project between the Secretariat and the BP Laboratory investigating the adoption of AQbD principles to Related substances tests and different formulations. The joint project would be used to demonstrate how applying the principles of AQbD could be used to develop improved and robust methods but without causing unnecessary burden to the Laboratory.

Supplementary Chapter The new Supplementary Chapter had been included in the BP 2022 and the expectation was that it would be regularly updated in future publications.

A large number of comments had been received on the draft text and the following major changes had been made: the title had been changed to "*Supplementary Chapter on the use of Analytical Quality by Design concepts for Analytical Procedures*" in order to highlight that the chapter was for guidance purposes and to be in line with ICH; the order of the various sections had been changed for clarity; reference to the existing guidance in Appendix III: Chromatographic Separation Techniques had been included.

The Supplementary Chapter emphasized the non-mandatory nature of the guidance and would be regularly updated to reflect any changes.

Membership of the AQbD Working Party Members endorsed the recommendation to invite five proposed new members to join the Working Party.

470 **Innovation Board** COM(21)25

Members were provided with an update on recent projects being undertaken by the joint BP-TSO Innovation Board.

Revision History The "Revision History" feature had been incorporated into monographs that had been revised in the British Pharmacopoeia 2022. This was linked to the existing track-changes feature and provided a short statement indicating the reason for the change to specific monograph tests.

OKO User Research The fourth round of user research had been completed in April and a summary of the key findings was presented. In addition to the targeted research a further survey had been sent out to users.

Several key areas identified from the combined research included: the wish for more direct contact with the BP; the value of increased international collaborations; suggestions to increase the profile of the BP within the healthcare system and to align with developments in the industry and healthcare sector through innovative areas of work. In addition, users would welcome the means to personalise the online version, enabling rapid access to frequently used areas of the site, they would also welcome tailored alerts to matters of

interest and the availability of other formats. There was a decreasing use of the hard copy publication, although it was still used in some countries.

Members supported the proposed areas for future development and were asked to provide any suggestions for future areas of research to the Secretariat.

471 **British Pharmacopoeia Laboratory** COM(21)26

British Pharmacopoeia Laboratory Reports The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the March 2021 meeting was provided for information.

British Pharmacopoeia Chemical Reference Substances Tables providing information on BPCRS up to the end of May 2021 were provided for information.

IV FUTURE PUBLICATIONS

472 **Nitrosamines: Production Statement Proposals** COM(21)27

The Secretariat had proposed two statements which were intended to alert the user to the potential risk of nitrosamine impurities in specific drug substances and products, but without creating additional burden to industry. These had been provided to Licensing colleagues on the MHRA's Nitrosamine Incident Management Team as it was critical that the BP was aligned with Licensing on this matter. Members were invited to discuss the proposals.

There was no perceived difference in the risk to the patient whichever approach was adopted and members agreed that including a Production statement in individual monographs was preferred over placing reliance on compliance with general monograph statements.

The Secretariat would be carrying out a short consultation in the autumn. This would allow sufficient time to make any changes required to reflect the latest situation and to include the statements in relevant monographs in the BP 2023.

V ANALYTICAL ISSUES

473 **Formulated Preparations: Tests for Loss on Drying/Water** COM(21)28

Introduction Several comments had been raised about the suitability of including tests for Water or Loss on Drying in monographs for formulated preparations. Such attributes were important for individual products but the value of including a generic requirement in a BP monograph was questioned, particularly in cases where wide limits were required to encompass all available licensed products.

Discussion The Water content of individual products would be controlled by the manufacturer and appropriate control measures would form part of the release and shelf-life specifications. It was suggested that the tests could be considered in a similar way to other quality tests that were critical to the performance of the product but could not readily be controlled within a monograph, for example the dissolution of prolonged-release formulations where the Production statement approach was used.

Members agreed that although tests for Water and Loss on Drying had previously been included in some formulation monographs, they should not be included routinely. However,

it was recognised that there could be exceptional circumstances where inclusion of a test was justified, for example if the active ingredient was hygroscopic, if water was used during the later stages of synthesis or due to the nature of the formulation. The Secretariat undertook to develop suitable policy guidelines with the default position that such tests should not usually be included.

474 **Aide Memoire and Policy List** COM(21)29

The Aide Memoire and Policy List were due to be updated by the end of the year. The Secretariat had identified several areas in the current guidance documents that should be updated to reflect new or amended policies and members were asked to identify any other aspects that should be addressed in the review. The Secretariat would provide draft updated versions for comment during the next few months with a view to providing finalised versions at the November meeting.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

475 **Expert Advisory Group PCY: Pharmacy** COM(21)30

The report of the EAG PCY meeting (29:05:20) was approved. This had been the final meeting of EAG PCY. Ongoing issues would be addressed within the newly formed EAG PCN: Pharmacy and Nomenclature in due course (minute 464 refers).

476 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(21)31

The report of the EAG HCM meeting (01:02:21) was approved. The EAG had received progress reports on several items and had reviewed the updated work programme. Monographs for herbal extracts had been prioritised for future work.

477 **Expert Advisory Group ABS: Antibiotics** COM(21)32

The report of the EAG ABS meeting (04:03:21) was approved and the following points were raised.

Oxytetracycline Preparations The EAG had questioned retention of the test for Light-absorbing impurities following inclusion of Related substances tests in these monographs. This would be considered as part of a wider review of monograph tests.

Ciprofloxacin Preparations; Titles The title of the new monograph for Ciprofloxacin Hydrochloride Eye Drops (licensed) had included the full name of the active ingredient in the title in order to distinguish it from the existing monograph for Ciprofloxacin Eye Drops (unlicensed) which contained Ciprofloxacin (as the lactate).

Aminoglycoside Antibiotic Product Monographs Several monographs would be added to the work programme with a view to including HPLC methods using pulsed amperometric detection. This would be a significant piece of work for EAG ABS over the next few years.

478 **Expert Advisory Group MC2: Medicinal Chemicals** COM(21)33

The report of the EAG MC2 meeting (05:05:21 and 07:05:21) was approved and the following points were raised.

Liothyronine Tablets; Related substances The EAG had discussed whether the high limit proposed by a company for Maillard impurities (impurities formed by reaction of the active ingredient with lactose present in the formulation) was justified, together with the need to ensure that the wide limits did not encourage poor practices in products where the impurity did not form.

Mebeverine Tablets; Dissolution One product had been unable to comply with the proposed limits for dissolution and it had been agreed that a more discriminatory test was required in order to avoid a test with very wide limits.

Solifenacin Preparations; Identification It had been agreed that better guidance on how to decide whether infrared spectra were concordant or not should be provided.

Mitoxantrone Sterile Concentrate; Acidity The pH varied across a range of formulations and it had been questioned whether it was appropriate to include pH limits in individual formulated preparation monographs or whether this aspect would be better addressed in general monographs.

Diclofenac Gel The current monograph had been expanded to cover formulations prepared from either Diclofenac Diethylamine or Diclofenac Sodium. A statement had been added at the head of the draft revised monograph highlighting that the two formulations were not interchangeable.

VII EUROPEAN PHARMACOPOEIA

479 **European Pharmacopoeia Update** COM(21)34

European Pharmacopoeia Commission Members discussed items from the 169th and 170th Sessions of the EP Commission and advised the UK Delegation accordingly.

Questionnaires sent to the UK National Authority A list of the recent questionnaires relating to proposals to add items to or remove items from the Ph Eur work programme was presented for information.

VIII INTERNATIONAL COLLABORATION

480 **International Update** COM(21)35

Members were provided with an update on international activities.

United States Pharmacopeia A teleconference with the USP had been held in May to discuss areas of mutual interest, including informal harmonisation projects for finished product monographs, standards for digital therapeutics, Analytical Quality by Design & method lifecycle and the pharmacopoeial response to the COVID-19 pandemic.

Chinese Pharmacopoeia Comments were awaited from China on the draft Memorandum of Understanding between the BP and the Chinese Pharmacopoeia.

Indian Pharmacopoeia Following the signing of the Memorandum of Understanding between the BP and the Indian Pharmacopoeia a useful teleconference had been held to progress areas of mutual interest. It was intended to hold more focused meetings in the future to concentrate on developing joint standards for small chemicals and antibiotics. The

partnership should support increased technical understanding and exchange of information between the two organisations.

Croatian Pharmacopoeia The Co-operation Agreement between the BP and the Croatian Agency for Medicinal Products and Medical Devices, which allowed the Croatian Pharmacopoeia to reproduce the BP general text on Unlicensed Medicines in their publication, had been extended until March 2026.

World Health Organization The WHO Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeial Specifications for Medicines had been held in May. Many topics had been discussed, including monographs and reference materials for the International Pharmacopoeia.

Regular meetings between representatives from the IMWP (International Meeting of World Pharmacopoeias) were still being held. Draft monographs for Favipiravir and Favipiravir Tablets (potential treatment for COVID-19) had been posted on the WHO website for comment and this had been highlighted on the BP website.

IX ANY OTHER BUSINESS

481 Titanium Dioxide

A member highlighted the recent statement issued by the European Food Safety Authority (EFSA) which stated that titanium dioxide was no longer considered safe when used as a food additive due to concerns over potential genotoxic effects. Although this statement specifically related to food grade material there could be implications for pharmaceutical grade material which was used in over 6000 licensed medicines to boost opacity and whiteness. There would be a huge impact on the industry if companies had to remove the material from their products and patients might become concerned if the appearance of established products changed.

Members would be kept informed of any developments.

482 Date of next meeting

Monday 8th November 2021.

FOR INFORMATION:

483 Items for Future Meetings

An updated list of items for discussion at future meetings was provided for information.