**SUMMARY MINUTES**

**of the**

**BRITISH PHARMACOPOEIA COMMISSION**

A meeting of the British Pharmacopoeia Commission was held at 151, Buckingham Palace Road, London SW1W 9SZ on Monday 14th November 2016.

**Present:** Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Professor M Almond, Dr J Beaman, Dr A M Brady, Dr G Cook, Dr A Gleadle (*lay member*), Dr R L Horder, Dr M G Lee, Mr R A Lowe, Dr B Matthews, Professor J Miller, Ms S Palser (*lay member*), Professor M Simmonds, Dr R Torano, Dr P Varley.

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

An apology for absence was received from Mr A Coulson.

Also present: Mrs M Barrett, Ms H Corns, Mr P Crowley, Miss A Gardiner, Mr A Gibb, Miss S Gomersal, Dr P Holland, Dr C Howard, Dr G Kemp, Dr R A Pask-Hughes, Mr J Pound and Mr S Young.

86 **Introductory Remarks**

**Welcome** The Chair welcomed Dr Gary Kemp, a new member of the Secretariat, and Ms May-Louise Wall, Pharmacopoeial Support Manager, who was attending the meeting as an observer.

**Staff News** Ms Catherine Pitt was currently on a six month secondment at the Department of Health. Ms Charlotte Hill had completed her time with the BP and Mr Jonathon Ware, DH, had taken over the digital project for six months.

Mrs Maria Barrett would be retiring on 16th December and so this would be her last meeting. Mrs Barrett had worked at the Secretariat since 2004 and had previously worked at the BP Laboratory for 14 years. On behalf of the BP Commission, the Chair thanked Mrs Barrett for her work over the years, particularly with regard to her role as Secretary to the UK delegation to the European Pharmacopoeia Commission.

**Annual Report** The Chair informed members that a letter had been received from Mr George Freeman, the former Minister for Life Sciences, thanking him for the 2015 Annual Report of the British Pharmacopoeia Commission and acknowledging the contribution from members throughout the year.

**British Pharmacopoeia 2017; British Pharmacopoeia (Veterinary) 2017; British Approved Names 2017** These items had been published during August and would come into effect on 1st January 2017.

**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 during the meeting. The Chair reminded members of the confidential nature of the meeting and that the papers should not be disclosed.

*Dr Torano declared an interest in one or more agenda items and appropriate action was taken.*

## I MINUTES

87 The minutes of the meeting held on 4th July 2016 were confirmed.

## II MATTERS ARISING FROM THE MINUTES

88 The following matters arising from the meeting held on 4th July 2016 were noted.

**Minute 64 British Pharmacopoeia Commission: Membership** The Chair requested that, in addition to the list of BPC members, the list of EAG members be included on the BP website.

**Minute 69 – Monograph Lifecycle Review: Development; Publication; Revision** In response to a request from the Chair, the Secretariat agreed to provide members with the full BP work programme at a future meeting.

**Minute 71 – Extemporaneous Preparations** Further discussions on this issue had been held at the autumn meetings of the Expert Advisory Groups on Pharmacy and Unlicensed Medicine and members would be kept informed of developments.

**Minute 72 – Soft Gel Paracetamol Capsules** This matter would be discussed at the EAG MC1 meeting in December and members would be updated at a future meeting.

**Minute 73 – Alkylsulfonate Esters: Production Statements in BP Monographs** This matter would be discussed at the EAG MC1 meeting in December and members would be updated at a future meeting.

## III REPORTS AND CORRESPONDENCE

***GOVERNANCE***

89 **BP Tender**

The contract for publication of future editions of the British Pharmacopoeia had been awarded to The Stationery Office.

90 **Update on the BP Digital Transformation Project** COM(16)43

Members were updated regarding the feasibility study on bringing the digital element of the BP publication in house. This work was being undertaken following the recommendations of the Triennial Review of the BP Commission and the BP Business Review.

91 **British Pharmacopoeia & Laboratory Services Group: Organisational Changes** COM(16)44

Members noted the recent changes to the British Pharmacopoeia & Laboratory Services group that had been introduced as a result of the BP business review.

***OPERATIONAL***

92 **Inhaled Products** COM(16)45

The Expert Advisory Group on Pharmacy had undertaken a review of the current BP policy on Inhaled Products. Mr Pound acknowledged the work undertaken by Miss Pitt and the

valuable contributions from members of EAG PCY. A number of meetings with the industry had also taken place.

**British Pharmacopoeia Monographs for Inhaled Products** A copy of the updated policy document was provided, which highlighted a number of changes in approach for BP monographs. The changes incorporated feedback that had been obtained since the policy had been established and were intended to bring the texts in line with European Pharmacopoeia monographs for Inhaled Products.

Members endorsed the revised policy, subject to any modifications required as a result of changes to the Ph Eur approach.

**Supplementary Chapter I O: Inhaled Products** The Supplementary Chapter had been updated to reflect the revised policy and was accepted.

**Preparations for Inhalation of the British Pharmacopoeia** Members endorsed the proposal to delete the BP General Monograph. The current test it contained, "*Content of active ingredient delivered by actuation of the valve*", would be transferred to a new BP Appendix which would ensure that it was only required if specified in a monograph.

93 **British Pharmacopoeia Laboratory** COM(16)46

**British Pharmacopoeia Laboratory Reports** The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the July 2016 meeting was provided for information. A table indicating progress on monograph reports since April 2016 and targets for 2017 was also provided.

**British Pharmacopoeia Chemical Reference Substances** A table providing information on BPCRS over the last six months was provided for information. This included details regarding the number of BPCRS in stock, the number of BPCRS out of stock and those awaiting procurement.

94 **Use of Unlicensed Medicines Monographs** COM(16)47

**Magnesium Glycerophosphate Oral Solution** The MHRA Defective Medicines Reporting Centre had received a report from a patient stating that after switching to a new supplier of an unlicensed medicine, they had experienced problems due to a lack of efficacy of the product. The BP/MHRA Laboratory had been asked to examine the product using the published BP Assay method (titration) and using Inductively Coupled Plasma-Mass Spectrometry to confirm the level of magnesium in the product and support the data generated using the published method. The testing had shown that an insufficient amount of magnesium was present in the product and a subsequent GMP Inspection had identified a manufacturing issue. This work highlighted the value of publishing monographs for unlicensed medicines and of collaboration with colleagues across the MHRA.

## IV FUTURE PUBLICATIONS

95 **Monograph Initiation: Candidate Monographs** COM(16)48

**Informal Harmonisation** The Secretariat had received requests to develop monographs for the following items via an informal harmonisation process with the USP: Caspofungin Acetate for Injection; Rotigotine Transdermal Patches. Members endorsed the addition of the two formulation monographs to the work programme.

**2015 PCA Prescribing Data and CMU Hospital Pharmacy Data** The Secretariat had examined the most recent lists of prescribed products provided by the NHS Information Centre and the Department of Health Commercial Medicines Unit. A number of items had been identified as potential candidate monographs from the top 600 most widely prescribed items and the top 200 items used in hospitals during 2015 and it was agreed that these should all be added to the work programme.

96 **Assays Based on the Results of Uniformity Tests** COM(16)49

A number of BP formulation monographs included Assays based on the average of the 10 individual results obtained in the test for Uniformity of content or Uniformity of dose. However, it had been pointed out that the Uniformity tests might have been carried out on 30 units if tested through the various levels permitted in the Appendices. At the recent meeting of the Expert Advisory Group on Pharmacy it had been agreed that the wording of such tests should be amended to: "*Use the average of the individual results determined in the test for Uniformity of content/delivered dose*". Members endorsed the recommendation of EAG PCY, subject to changing "determined" to "obtained".

97 **Approved Synonyms** COM(16)50

**New monographs** The proposed new Approved Synonym relating to an item added to the European Pharmacopoeia by means of the 9th Edition was approved. This item would be added to Appendix XXI B in the BP 2018 and would be incorporated within the online updates to the BP 2017. For the remaining new monographs in the 9th Edition and in Supplement 9.1, members recommended that the Ph Eur titles should be used.

**Title changes** The title of the monograph for Pholcodine had been changed to Pholcodine Monohydrate. Members endorsed the recommendation that the change in title should be reflected in the BP.

**British Approved Names** As a consequence of additions to the Ph Eur, the following changes would be made in a future BAN publication: Tacalcitol Monohydrate and Gadodiamide Hydrate would be added as new British Approved Names (Modified) to the entries for Tacalcitol and Gadodiamide respectively.

98 **British Pharmacopoeia 2018: Text Review Dates; Comments Arising from BP 2017 Text Review** COM(16)51

**BP 2018 Text Review Dates** Dates for reviewing the BP 2018 text using the document review tool (DRT) had been agreed within the Secretariat and the dates relating to the review by Commission were provided for information. As for the previous edition, two batches of text would be posted on the DRT. Members would be given two weeks to review the text, after which the Secretariat would examine the comments received and provide feedback to members on action taken.

**BP 2017 Editorial Style**

A number of inconsistencies had been noted during review of the BP 2017 text. These were brought to the attention of members, together with some points raised at previous meetings.

***Information in Chromatographic Tests***

***Retention times; Related substances*** The current policy to quote relative retentions, rather than absolute retention times, was confirmed.

***Assay*** It was suggested that including an absolute retention time under Assay would be useful for the analyst.

***Standard requirements*** The current policy to specify limits for standard requirements, such as those for symmetry factor, only when they fell outside the default Appendix limits was confirmed.

## V ANALYTICAL ISSUES

### 99 Use of Thermal Gravimetric Analysis COM(16)52

A paper prepared by the BP/MHRA Laboratory was presented which outlined a proposal to use Thermal Gravimetric Analysis (TGA) as an alternative to traditional Loss on drying (LOD) methods during the routine testing of British Pharmacopoeia Chemical Reference Substances. The main advantages to using TGA were the use of a much smaller sample size and a reduced analysis time. It was noted that the technique was not intended to replace the use of the Karl Fischer method for Water determination and was not intended to replace LOD methods in BP monographs.

Members supported the proposed move away from LOD methods and endorsed the recommendation to use TGA as an alternative to traditional Loss on drying methods for BPCRS analysis.

## VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

### 100 Expert Advisory Groups, Panels of Experts and Working Parties COM(16)53

**New Members** Mr Blake, Dr Reich and Dr Sherwin had accepted the invitations to join EAGs ABS, HCM and the AQbD Working Party respectively.

**Expert Advisory Groups NOM: Nomenclature and PCY: Pharmacy** Following the resignation of the former representative from the British National Formulary, Ms Angela McFarlane (Clinical Writer, BNF) had been nominated as the new representative from the BNF. Members endorsed the recommendation to appoint Ms McFarlane to EAG NOM and EAG PCY.

**Expert Advisory Group ULM: Unlicensed Medicines** Mr Sean Jones had resigned from EAG ULM due to conflicting work commitments. Dr Marion Westwood (MHRA) had been recommended as the new representative from the Licensing Division and had attended the recent ULM meeting. Members endorsed the recommendation to appoint Dr Westwood to EAG ULM.

### 101 Expert Advisory Group ULM: Unlicensed Medicines COM(16)54

The report of the EAG ULM meeting (21:4:16) was approved and the following points were raised.

**Policy for Transferring Monographs to EAG ULM** The proposals had been endorsed at the July meeting (minute 70 refers) when it had been agreed that any monographs should be reviewed by the relevant EAG before being transferred to EAG ULM.

**Supplementary Chapter V F: Aseptic Preparation of Unlicensed Medicines** The Chapter had been included in the British Pharmacopoeia 2017. It was agreed that the

Secretariat should inform the Chemistry, Pharmacy and Standards Expert Advisory Group of the Commission on Human Medicines that the information had been published.

102 **Expert Advisory Group MC1: Medicinal Chemicals** COM(16)55

The report of the EAG MC1 meeting (6:6:16) was approved.

103 **Panel DNA: Identification Techniques** COM(16)56

The report of the Panel DNA meeting (8:6:16) was approved. This had been the last meeting that Dr Helliwell (Chair) would attend and tributes had been paid for his contribution to the herbal project and for his long-standing service to the BP. The Chair also asked that his thanks to Dr Helliwell be placed on record.

The Herbals project had been expanded to cover phytochemical analysis and a further staff member had been appointed to the Herbals team. Members were informed that work was progressing towards implementation of the ISO 9001 Quality System within the BP-NIBSC Laboratory. The Panel had received the first report obtained using Next Generation Sequencing and this had been well received.

104 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(16)57

The report of the EAG HCM meeting (21:6:16) was approved and the following point was raised.

**Peppermint Spirit** The current monograph did not contain any tests to determine the identity or chromatographic profile of the components and licensed products did not appear to be available. Members endorsed the recommendation of EAG HCM to omit the monograph from the next edition of the BP.

105 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(16)58

The report of the *ad-hoc* EAG BIO meeting (20:7:16), which had been arranged to discuss the BP's future direction for biological medicines, was approved.

106 **Expert Advisory Group PCY: Pharmacy** COM(16)59

The report of the EAG PCY meeting (12:9:16) was approved and the following points were raised.

**Dissolution** Issues such as the appropriateness of the current Q-value and the continued Production statement approach for prolonged-release preparations had been discussed. The Secretariat was currently consulting with stakeholders and further discussions would be held before proposals were submitted to the Commission.

**Doxorubicin Injection** It had been agreed to replace the current monograph by two separate monographs for Sterile Doxorubicin Concentrate and Doxorubicin Hydrochloride for Injection to reflect the products available. As the dry powder formulation could be administered either by injection or infusion, EAG PCY had been asked to advise on the most suitable monograph title. At the meeting it had been agreed that the title should be in the form "Doxorubicin for Injection/Infusion", in accordance with the EDQM Standard Term and this recommendation had been drawn to the attention of the Expert Advisory Group on Antibiotics. However, as this approach was against BP Commission policy for naming monographs the Secretariat had recommended that the main title should be Doxrorubicin Injection and that Doxorubicin Infusion should be included as a subsidiary title.

107 **Expert Advisory Group ABS: Antibiotics** COM(16)60

The report of the EAG ABS meeting (21:9:16) was approved and the following points were raised.

**Tigecycline for Injection** The draft injection monograph was ready for publication, but the corresponding Ph Eur monograph for the active substance had not yet been published.

**Marbofloxacin Preparations** In view of the number of monographs for veterinary medicines that fell under the remit of EAG ABS, members had agreed that it would be useful to appoint a representative from the Veterinary Medicines Directorate to the EAG.

## VII EUROPEAN PHARMACOPOEIA

108 **European Pharmacopoeia Update** COM(16)61

**European Pharmacopoeia Commission** The draft report of the 155th Session of the EP Commission (June 2016) had been posted on the BP website. The 156th Session would be held in November 2016.

**Questionnaires sent to the UK National Authority** Members were informed that national pharmacopoeial authorities regularly received questionnaires from the EDQM seeking information on whether or not products were licensed and/or on the market, with a view to recommending whether items should be added to or removed from the Ph Eur work programme or whether monographs should be suppressed in future publications. The Secretariat made enquiries and sought advice, as appropriate, before sending a response on behalf of the UK delegation. Examples of recent requests had been provided for information.

## VIII INTERNATIONAL COLLABORATION

109 **EU Referendum** COM(16)62

Following the EU Referendum, the MHRA was working closely with the Government to ensure the continued safe and effective regulation of medicines and medical devices in the UK. While the negotiations were being undertaken the UK would remain a full and active member of the EU with all the rights and obligations of EU membership in place.

110 **International Collaboration** COM(16)63

Members were provided with an update on international activities.

**Japan** Dr Atkinson and Ms Corns had attended the WHO 7th International Meeting of World Pharmacopoeias, which had been hosted by the Japanese Pharmacopoeia in Tokyo. The main text of the Good Pharmacopoeial Practices had been signed off by the WHO Expert Committee on Pharmaceutical Preparations. Good progress had been made with the technical annex on Compounded Preparations and work was in progress on the draft text relating to Herbal Medicines. A number of items had been identified for discussion at future meetings.

The GPhP meeting had been followed by the 130th Symposium of the Japanese Pharmacopoeia and a number of bilateral meetings had been held during the visit.

***PMDA*** A meeting had been held with representatives from the Pharmaceutical and Medical Devices Agency to exchange information on the development of monographs.

***Indian Pharmacopoeia*** The potential for future staff exchanges had been discussed to develop relationships between the BP and IP and to aid future harmonisation projects.

***Brazil*** A draft Memorandum of Understanding between the BP and the Brazilian Pharmacopoeia was currently in preparation.

***Ukraine*** Information had been provided on the BP monographs that had been incorporated within the State Pharmacopoeia of Ukraine.

**Estonia** Mr Pound, Mr Gibb and Ms Pitt had attended the EDQM International Conference held in Tallinn, Estonia, which had been arranged to promote the 9th Edition of the European Pharmacopoeia. A significant part of the conference had been devoted to biological materials and a number of workshops had been held.

**China Chamber of Commerce for Import and Export of Medicines and Health Products** Mr Evans had attended a meeting between the MHRA and representatives from CCCMHPIE and China industry. A number of items had been discussed, including the registration of traditional herbal medicines, Licensing and Inspection requirements, BP monographs for THM and how CCCMHPIE can help with this work.

**WHO Geneva** Dr Holland and Mr Evans had attended the 63rd Consultations on International Non-proprietary Names. Over 50% of the names discussed were for biological products. Dr Holland would be retiring as Chair and member of the INN Expert Committee and this had been her last meeting. The group had paid tribute to her services to the Committee for many years. Mr Evans would continue to attend future meetings as an observer.

Ms Corns had attended the 51st Expert Committee on Specifications for Pharmaceutical Preparations. The meeting had covered a wide range of WHO activities including the International Pharmacopoeia and guidance on substandard/spurious/falsely-labelled/falsified/counterfeit medicines.

**Joint Compendial Meeting** Dr Holland, Ms Gomersal and Ms Lockie-Williams had participated at this meeting (teleconference). An online presentation had been provided on BP herbal monographs and the BPNARM project, together with an update on current and future BP activities. Positive feedback had been received regarding the ability of users to comment on draft text via the BP website.

**International Harmonisation with the USP** The BP had been collaborating with the USP as part of the USP "up to date programme" to try and ensure harmonisation of revised monographs. A number of monograph projects had been identified and lead pharmacopoeias assigned (BP or USP).

## IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

111 **Future meetings** A number of presentations had been made at recent meetings and this was likely to continue as a way to engage with members.

## X ANY OTHER BUSINESS

112 **Date of next meeting** Wednesday 8th March 2017.