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 Wednesday 8th March 2017.

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

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

Apologies for absence were received from Dr A M Brady, Mr R A Lowe, Dr B Matthews and Dr P Varley.

Also present: Ms H Corns, Ms E Cotterill, Mr L Elanganathan, Mr A Evans, Dr A Gardiner, Mr A Gibb, Mr L Gibson, Ms C Gkouva, Miss S Gomersal, Dr P Holland, Dr G Kemp, Mr J Pound, Ms M L Wall, Mr J Ware, Mr M Whaley and Mr S Young. Mr P Crowley attended the meeting for the items recorded under minutes 127 to 141.

113 **Introductory Remarks**

Welcome The Chair welcomed Mr Gibson and Ms Gkouva from the BP-NIBSC Herbals Laboratory and Mr Elanganathan, a temporary member of the Secretariat. He also welcomed Mr Ware (current fast streamer) and Ms Cotterill (new fast streamer).

Staff News Dr Rosemary Pask-Hughes had left the Secretariat at the end of January. Dr Pask-Hughes had worked at the Secretariat since 1984, with a six year break. She had been involved with a number of Expert Advisory Groups during her time with the BP, most notably with the EAG on Biological and Biotechnological Products and her expertise would be greatly missed. The Chair wished to place on record the Commission's thanks to Dr Pask-Hughes.

This would be the last meeting for Dr Patience Holland, who would be leaving the Secretariat at the end of June, after nearly 28 years of service. Dr Holland had been involved with a number of Expert Advisory Groups over the years, including those on Nomenclature and on Herbal and Complementary Medicines. She had represented the UK on the WHO INN Committee for many years and had recently held the post of Chair of that Group. She had been instrumental in establishing Panel DNA (Identification Techniques) and her expertise would be missed. On behalf of the BP Commission, the Chair thanked Dr Holland for her contribution to the work of the BP and wished her well for the future.

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 Cook declared an interest in one or more agenda items and appropriate action was taken.

I MINUTES

114 The minutes of the meeting held on 14th November 2016 were confirmed.

II MATTERS ARISING FROM THE MINUTES

115 The following matters arising from the meeting held on 14th November 2016 were noted.

Minute 88 – Monograph Lifecycle Review; BP Work Programme The Secretariat was currently considering the best way to present the BP work programme to members and this would be provided at a future meeting.

Minute 92 - Inhaled Products; Minute 96 – Assays Based on the Results of Uniformity Tests The changes agreed at the last meeting would be included in the BP 2018.

Minute 98 – BP 2017 Editorial Style: Information on Chromatographic Tests It had been questioned whether there was any reference to the mandatory status (or otherwise) of retention times included in the BP. Members were informed that within the Supplementary Chapter on "Control of Impurities" (I A), there was a section on retention times and relative retentions which confirmed the current approach of quoting retention times as "about X minutes". It also stated that "identification of peaks is generally not based on absolute retention times since these may be too system dependant".

Minute 101 – Supplementary Chapter V F: Aseptic Preparation of Unlicensed Medicines The Chemistry, Pharmacy and Standards Expert Advisory Group of the Commission on Human Medicines had been informed that the Chapter had been published in the BP 2017.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

116 **BP Tender**

The contract with The Stationery Office for publication of future editions of the British Pharmacopoeia had been signed.

117 **MHRA Strategy for Pharmacopoeial Quality Standards for Biological Medicines** COM(17)1

Development of the Strategy and Public Consultation In view of the increasing importance of biological medicines, and the role of pharmacopoeial standards in the wider agency, the MHRA Corporate Executive Team (CET) had endorsed the development of an Agency-wide strategy. A public consultation had been launched in January, and was open until 10th April, and a news item had been posted on the MHRA website. Members were encouraged to share details of the consultation with interested parties.

Stakeholder Engagement Strategy Over 200 potential national and international stakeholders had been identified and discussions had been held with a number of key stakeholders either face-to-face or in WebEx meetings. The consultation had also been promoted by MHRA staff attending external events and articles had been published in a number of relevant publications. Once the consultation period had ended, the Secretariat would analyse the comments and a formal response would be issued. The outcome would

be brought to members' attention at a future meeting and stakeholders would be informed accordingly.

USA Meetings Dr Atkinson, Mr Pound and Mr Gibb had recently visited the USA and had discussed the biological strategy at meetings with representatives from the United States Pharmacopeia (USP), the US Food and Drug Administration (FDA) and the pharmaceutical industry. Colleagues from NIBSC had also been present at these meetings.

118 **Update on the BP Digital Transformation Project** COM(17)2

Mr Ware gave a presentation outlining the progress that had been made with regard to the feasibility study on bringing the digital element of the BP publication in house.

OPERATIONAL

119 **BPC and EPC: Ways of Working** COM(17)3

A survey had been undertaken in December 2016 seeking members' views on current ways of working and on how these could be improved. Comments had been sought regarding meetings of the British Pharmacopoeia Commission and on UKD briefing meetings.

A number of suggestions for improvement had been made and the Secretariat agreed to introduce minor changes over the course of the next few meetings to address these issues.

120 **British Pharmacopoeia Laboratory** COM(17)4

British Pharmacopoeia Laboratory Reports The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the November 2016 meeting was provided for information.

British Pharmacopoeia Chemical Reference Substances Tables providing information on BPCRS activity over the last few months were provided for information.

IV FUTURE PUBLICATIONS

121 **British Pharmacopoeia 2018 Publications** COM(17)5

BP 2018 The Secretariat was currently preparing text for inclusion in the British Pharmacopoeia 2018 and the British Pharmacopoeia (Veterinary) 2018. All items included in the 9th Edition of the European Pharmacopoeia, together with those from Supplements 9.1 and 9.2, would be incorporated in either the BP 2018 or the BP (Vet) 2018, as appropriate. The 2018 publications would be published in August 2017 and would come into effect on 1st January 2018.

Electronic updates The text from the Ph Eur 9th Edition had been added to the online BP in December, in advance of its implementation on 1st January 2017. The text from Supplements 9.1 and 9.2 would be available in advance of their implementation dates (1st April 2017 and 1st July 2017 respectively).

Preliminaries Members recommended that the British Pharmacopoeia 2018 and the British Pharmacopoeia (Veterinary) 2018 should be published and confirmed that the draft Prefaces to both publications were acceptable.

Technical/Editorial Changes

Inhaled Products The changes noted at the last meeting would be incorporated in the BP 2018: Supplementary Chapter I O would be revised to reflect updated policy guidelines; the General Monograph on Preparations for Inhalation of the British Pharmacopoeia would be deleted and the specific test transferred to a new BP Appendix; existing monographs would be updated in accordance with the new style template.

Uniformity of content; Uniformity of dose The agreed changes to the wording of Uniformity tests would be made to about 60 monographs in the BP 2018.

122 **Monographs for Omission from the BP 2018 and BP (Vet) 2018** COM(17)6

Since publication of the BP 2017 publications, a number of monographs had been identified as candidates for omission from the BP 2018 publications. In accordance with usual practice, the Secretariat would contact countries in which the BP was used, including Australia, to ascertain if the products were still available / used before finalising the list. Members endorsed the recommendation to omit the monographs from the BP 2018 and the BP (Vet) 2018. In accordance with regulation 252 (2c) of the Human Medicines Regulations 2012, these monographs would continue to remain in force.

123 **Approved Synonyms** COM(17)7

New monographs The proposed new Approved Synonym relating to an item added to the European Pharmacopoeia by means of Supplement 9.2 to 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 Supplement 9.2, members recommended that the Ph Eur titles should be used.

British Approved Names As a consequence of additions to the Ph Eur, Milbemycin Oxime would be added as a new British Approved Name in a future BAN publication.

124 **British Approved Names 2017: Supplement No. 1** COM(17)8

Supplement No. 1 to British Approved Names 2017, containing 47 new names, had been prepared and a copy was provided for confirmation. The text had been agreed by the Expert Advisory Group on Nomenclature and had been sent to manufacturers for comment. All the entries were either recommended International Nonproprietary Names (rINN) which had UK product licences or were Ph Eur monograph titles which had previously been approved for inclusion in the list of BANs. Members were invited to examine the draft and to send any comments to the Secretariat by **22nd March**.

Subject to any comments received, the Commission approved the content of the draft Supplement and recommended that it should be published.

V ANALYTICAL ISSUES

125 **Introduction of New Analytical Technologies** COM(17)9

Background It had previously been agreed that consideration should be given to including diode array detection as a means of Identification in BP monographs. After further consideration within the Secretariat this item had been expanded to address how the BP could best respond to the increased use of new analytical techniques whilst acknowledging that pharmacopoeial monographs should specify well-established techniques using readily available equipment and reagents.

Proposed action The Secretariat had proposed that an *ad-hoc* group should be established with the objective of developing a framework for introducing new techniques into the BP which would encompass the identification, evaluation and timely introduction of such techniques.

Discussion Members supported the proposed actions, but a number of reservations were expressed. It was appropriate and timely for the BP to consider the inclusion of new and improved techniques, but it was recognised that pharmacopoeial methods should be able to be carried out routinely.

The Secretariat agreed to identify potential members with a view to presenting names and proposed ways of working at the next meeting.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

126 **Expert Advisory Groups, Panels of Experts and Working Parties** COM(17)10

New Members Ms McFarlane and Dr Westwood had accepted the invitations to join EAGs PCY and ULM respectively.

Changes to Chairs / Vice-Chairs A number of changes had recently been made following discussions with the relevant EAG/Panel Chairs and Vice-Chairs and the individuals concerned and these were endorsed by members.

Dr Brady had agreed to take on the role of Vice-Chair of EAG BIO.

Professor Simmonds had agreed to take on the role of Chair of EAG HCM.

Dr Richard Middleton had agreed to take on the role of Vice-Chair of EAG HCM.

Professor Almond had agreed to take on the role of Vice-Chair of EAG MC3.

New representatives from the MHRA and NIBSC A number of changes to MHRA/NIBSC representation had recently been made and these were endorsed by members.

Dr Melanie Pires had been appointed as the new Licensing representative on EAG ABS.

Dr Karin Nordgren (NIBSC, UK expert on the EDQM Bacterial Endotoxins Working Party) had been appointed as a Specialist member of EAG BIO.

Dr David Deutsch had been appointed as the new alternate Licensing representative on EAG MC1.

Mrs Christine Gray had been appointed as the new representative from the Inspectorate on WP AQbD.

Expert Advisory Group HCM: Herbal and Complementary Medicines Members endorsed the recommendation to appoint Dr Eike Reich (Head of Laboratory, CAMAG, Switzerland) as a full member of EAG HCM.

Expert Advisory Group ULM: Unlicensed Medicines Members endorsed the recommendation to appoint Ms Sarah Hartley (Analytical R+D, Rosemont [Perrigo]) to EAG ULM.

Working Party AQbD: Analytical Quality by Design Members endorsed the appointment of Mr Brent Harrington (Director of Statistics, Pfizer, USA) as a corresponding member of WP AQbD.

Retired Members The following members had resigned in recent months: Mr Paul Ellis (EAG ABS), Dr Lucy Findlay (EAG BIO), Professor Annie Bligh (EAG HCM), Dr James Ballinger and Dr Steven Waters (Panel RAD). Letters of thanks had been or would be sent thanking the former members for their past service to the work of the BP.

127 **Expert Advisory Group MC3: Medicinal Chemicals** COM(17)11

The report of the EAG MC3 meeting (28:9:16) was approved and the following point was raised.

Rotigotine Transdermal Patches; Dissolution The EAG had recommended inclusion of a Production statement, in line with that included in monographs for prolonged-release preparations, rather than a specific dissolution test. It was pointed out that the inclusion of a Production statement was not always the best approach and that this aspect was being considered as part of the review of dissolution testing currently out for consultation.

128 **Working Party AQbD: Analytical Quality by Design** COM(17)12

The report of the WP AQbD meeting (3:10:16) was approved. A workshop had subsequently been held to evaluate the scope of the project and the work carried out to date. A report would be presented at a future meeting.

129 **Expert Advisory Group ULM: Unlicensed Medicines** COM(17)13

The report of the EAG ULM meeting (20:10:16) was approved and the following points were raised.

Cefuroxime Intracameral Injection There had been a general consensus that content limits of 95.0 to 105.0% might be too stringent for unlicensed formulations, particularly for reconstituted preparations. It had been agreed that EAG ULM should consider whether additional policy guidelines should be developed.

Nadolol Oral Suspension; Nifedipine Oral Suspension A member of the EAG had arranged for practical evaluation of these new monographs to be undertaken by university students.

130 **Expert Advisory Group MC2: Medicinal Chemicals** COM(17)14

The report of the EAG MC2 meeting (1:11:16) was approved and the following point was raised.

Methylphenidate Preparations; Related substances The Laboratory had found that extended extraction times were required in order to enable the active substance to be extracted from the prolonged-release capsule and tablet formulations.

131 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(17)15

The report of the EAG HCM meeting (23:11:16) was approved.

132 **Expert Advisory Group MC1: Medicinal Chemicals** COM(17)16

The report of the EAG MC1 meeting (6:12:16) was approved and the following points were raised.

Paracetamol Capsules In accordance with the preferred approach of the Commission, separate dissolution tests for hard and soft gel capsules had been drafted for inclusion and the revised monograph would be included in the BP 2018.

Alkylsulfonate Esters: Production Statements in BP Monographs At the July 2016 meeting, it had been agreed that further information should be sought before accepting the recommendations of EAG MC1 to include a Production statement in relevant BP formulation monographs.

It was agreed that, subject to the receipt of further information and discussions with Licensing on the appropriate wording, the BP should aim to include Production statements in relevant monographs in a future publication.

VII EUROPEAN PHARMACOPOEIA

133 **European Pharmacopoeia Update** COM(17)17

European Pharmacopoeia Commission The draft report of the 156th Session of the EP Commission (November 2016) had been posted on the BP website.

The 157th Session would be held on 21st and 22nd March.

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

134 **International Collaboration** COM(17)18

Members were provided with an update on international activities.

Chinese Pharmacopoeia During 2015 two members of staff from NIBSC associated with the BP-NIBSC Herbals project had visited the Chinese Pharmacopoeia. In a reciprocal arrangement, a member of staff from the Chinese Pharmacopoeia would be visiting the MHRA for 4 weeks in March/April and would be spending two weeks at the MRHA and two weeks at NIBSC.

India Dr Atkinson had visited India in January as part of an MHRA delegation with Mr Gerald Heddell (Head of Inspection, Enforcement and Standards) and Mr Ian Hudson (Chief Executive of the MHRA). A productive meeting had also been held with representatives from the Indian Pharmacopoeia Commission where discussions had been held regarding potential collaborative working on monographs and staff exchanges. A Memorandum of Understanding between the BP and the IP had been drafted which would

facilitate future collaborations. In addition, progress had been made regarding the provision of herbal samples for testing.

Kazakhstan; Ukraine New Memoranda of Understanding had recently been signed with the State Pharmacopoeia of the Republic of Kazakhstan and the State Pharmacopoeia of Ukraine which allowed the verbatim reproduction of a set number of BP monographs, including reference to BPCRS.

United States Pharmacopeia A teleconference had been held in January with the USP to discuss progress on the ongoing collaboration project to revise outdated monographs. Five groups of monographs had been selected for revision and BP/USP representatives had been nominated to lead the work in specific areas.

USP and European Compliance Academy (ECA) Joint Conference on Lifecycle Approach of Analytical Procedures Mr Pound and Mr Crowley had attended a conference in Prague (November 2016) at which Mr Pound had given a presentation on the joint BP/MHRA feasibility study on Analytical Quality by Design. This work was seen to aid innovation and information sharing. The discussions between the BP and the USP were considered a good example of compendia working together to share knowledge and developments in this area. The attendees were keen to see how the laboratory evaluations would be referenced in a monograph.

WHO Good Pharmacopoeial Practices The main GPhP document had been finalised in April 2016. A number of additional sections were still in preparation or had not been started. It was understood that a survey would be sent to stakeholders about the document.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

135 **EU Referendum** The MHRA was continuing with business as usual and were considering the implications of Brexit for the agency.

136 **Mutual Recognition of Inspections** The EU had signed an agreement with the US Food and Drug Administration which enabled mutual recognition of inspections conducted within the EU and the USA.

137 **Accommodation** The MHRA would be relocating to a site in Canary Wharf, London, during 2018.

138 **Laboratory** The current contract with the Laboratory of the Government Chemist would end in 2021.

X ANY OTHER BUSINESS

139 **Annual Report of the British Pharmacopoeia Commission** The Chair thanked those members who had provided comments on the draft Annual Report. The report would be published later in the year.

140 **Appraisals** The Chair said he intended to carry out the annual appraisals during April or May and details would be provided shortly.

141 **Date of next meeting** Monday 3rd July 2017.