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 Tuesday 14th November 2017.

Present: Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Professor M Almond, Dr J Beaman, Dr A M Brady, Dr G Cook, Mr A Coulson, 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 and Dr P Varley.

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

Also present: Ms H Corns, Mr P Crowley, Mr L Elanganathan, Mr A Evans, Dr A Gardiner, Mr A Gibb, Ms S Gomersal, Dr C Howard, Dr G Kemp, Dr C Lenihan, Mr S Maddocks, Mr H Makwana, Mr J Parker, Dr K Radi, Ms M L Wall, Mr M Whaley and Mr S Young.

Mr A Bartlett attended the meeting for the item recorded under minute 167.

166 **Introductory Remarks**

Welcome The Chair welcomed Mr Maddocks and Mr Makwana (new members of the Secretariat) and Mr Parker (new fast streamer from the Department of Health). He also welcomed back Dr Howard, who had returned after maternity leave.

Professor Derek Calam OBE CBE Members had been saddened to learn of the death of Professor Derek Calam, a former Chair of the BP Commission.

The Commission observed a minutes silence in remembrance of Professor Calam.

Membership This was the last meeting for Dr Horder, who had been a member of the BP Commission since 2002. The Chair paid tribute to Dr Horder and thanked him on behalf of the Commission for his significant contribution over the years both in terms of the BP Commission directly and in his roles as Chair of the Expert Advisory Groups on Antibiotics and Pharmacy and as Chair of the Ph Eur Expert Group on Dosage Forms and Methods and as alternate member of the UK delegation. Dr Horder thanked the Chair for his kind words and said that he had enjoyed his time with the BP and EP over the years. He would continue to be involved with some pharmacopoeial activities.

Chair Members were pleased to note that Professor Taylor had been appointed for a second term as Chair of the BP Commission (1 October 2017 to 30 September 2021).

British Pharmacopoeia 2018; British Pharmacopoeia (Veterinary) 2018; Supplement No. 1 to British Approved Names 2017 These items had been published in August and would come into effect on 1st January 2018.

British Pharmacopoeia Commission Annual Report for 2016 The Annual Report for 2016 of the Medicines Advisory Bodies had been laid before Parliament on 19th July 2017 and was available via the BP website and the GOV.UK site.

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.

167 **Brexit**

The Chair welcomed Mr Adrian Bartlett (EU Policy manager, Medical Devices) who provided an update on how the MHRA was preparing to deal with the outcome of Brexit.

I MINUTES

168 The minutes of the meeting held on 3rd July 2017 were confirmed.

II MATTERS ARISING FROM THE MINUTES

169 The following matters arising from the meeting held on 3rd July 2017 were noted.

Minute 147 – General Principles for Finished Product Monographs of the European Pharmacopoeia A response outlining the Commission's position had been sent to the EDQM as agreed.

Minute 152 – New Analytical Technologies: *Ad-hoc* Group Members were informed that the role and remit of the *ad-hoc* group would be defined as the Content Strategy developed.

Minute 155 – EAG MC3 Minutes: Quetiapine Preparations Reference to the minimum resolution of 1.5 had been included in the updated Aide Memoire as agreed.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

170 **Declaration of Interests**

Members were reminded of the requirement to complete an annual declaration of interests form. The form relating to interests during the past year would shortly be circulated and members were asked to return the signed forms to Dr Swanson by the requested deadline.

171 **BP Transformation Project** COM(17)32

Members were provided with an update on the various aspects of the BP Transformation Project.

172 **MHRA Strategy for Pharmacopoeial Quality Standards for Biological Medicines: Update** COM(17)33

Introduction The comments received in response to the public consultation had been analysed and a formal response from the MHRA had been published on the GOV.UK website (and the BP website) on 23rd October. A copy was provided for information. Mr Gibb thanked those members of the Commission and the Expert Advisory Group on Biological and Biotechnological Products for their input throughout the whole process.

Response document Dr Gardiner gave a presentation which outlined the consultation process, the outcomes and next steps. The responses received had led to the identification of a number of key themes, which would be addressed during the next stages.

Vision Statement; Work Programme The vision statement had been amended to reflect the outcome of the consultation. In order to implement the biologicals strategy the future work programme had been split into three key areas of activity: (i) standards development; (ii) engaging with users and building knowledge; (iii) working with international peers.

Next steps It was intended that a series of stakeholder meetings would be held to discuss issues further. EAG BIO would continue to engage with stakeholders, including providing regular updates to the BP Commission. As Chair of EAG BIO, Dr Varley said he had been very pleased at the success and outcomes of the consultation and that the group would start to implement the new work programme at the next BIO meeting.

173 **Content Strategy Update**

Ms Corns gave a presentation outlining the work carried out on the development of a strategy relating to the content of the BP.

OPERATIONAL

174 **Split Standard Terms** COM(17)34

The current policy for naming monographs for Prolonged-release/Chewable/ Dispersible/ Soluble preparations was to split the standard term, resulting in titles in the form "Prolonged-release ACTIVE Capsules", "Chewable ACTIVE Tablets", etc. Following a request by the Expert Advisory Group on Nomenclature, the Pharmacy EAG had recommended that the title of affected monographs should be changed to reflect the current regulatory requirements for naming medicines. The standard term should not be split and titles would be in the form "ACTIVE Prolonged-release Capsules", "ACTIVE Chewable Tablets", etc.

Members endorsed the recommendation that this approach should be adopted for all relevant NEW monographs included in the BP 2019 onwards. For existing affected monographs (about 105) it was agreed that the title change should be made at the time of general revision and that any outstanding monographs should be updated over a 5-year period and members concurred. In accordance with BP policy the former title would be included as a subsidiary title in affected monographs.

175 **Dispensing and Supply Statements** COM(17)35

There were a number of monographs in the BP which contained statements in the form "*When [product name] is prescribed or demanded, [monograph title] shall be dispensed or supplied*". These usually related to monographs where the item was also known by a title other than the monograph title (but there was no subsidiary title) or where a particular strength was specified. As information on prescribing was not within the remit of the BP, and in view of the fact that some of the statements might not reflect current practices, the Expert Advisory Group on Pharmacy had recommended that a widespread consultation should be undertaken to ascertain whether these statements should be retained or removed from the affected monographs. A stakeholder consultation had been carried out (December 2016 to January 2017) and the various responses had been considered at the recent PCY meeting.

Although there had been some support for retaining the statements, the majority of the responses had indicated that they could be removed as users were unlikely to look for prescribing information in the BP.

Members endorsed the recommendation to remove all the statements from the BP and BP (Vet) at the earliest opportunity.

176 **British Pharmacopoeia Laboratory** COM(17)36

British Pharmacopoeia Laboratory Reports The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the July 2017 meeting was provided for information.

British Pharmacopoeia Chemical Reference Substances Tables providing information on BPCRS up to the end of September 2017 were provided for information.

IV FUTURE PUBLICATIONS

177 **Work Programme** COM(17)37

Background The Secretariat had provided a consolidated work programme which included the full list of new and revised monographs for each of the monograph-producing Expert Advisory Groups and Panels of Experts and would enable the Commission to gain a better oversight of the overall BP work programme.

Discussion Members were pleased to receive the information and agreed that the format and level of information on monographs was appropriate. The information changed throughout the year and the Secretariat had proposed providing an annual update, which was accepted.

178 **Approved Synonyms** COM(17)38

New monographs The proposed new Approved Synonym relating to an item added to the European Pharmacopoeia by means of Supplement 9.3 to the 9th Edition was approved. This item would be added to Appendix XXI B in the BP (Vet) 2019 and would be incorporated within the online updates to the BP 2018.

The new Ph Eur monograph for Tylosin Phosphate for Veterinary Use (approved synonym - Tylosin Phosphate) had necessitated a change to the current approved synonym for Tylosin Phosphate Bulk Solution for Veterinary Use. The proposed change to Tylosin Phosphate Bulk Solution was accepted.

For the remaining new monographs in Supplements 9.3 and 9.4, members recommended that the Ph Eur titles should be used.

Title changes The title of the monograph for Metoclopramide Hydrochloride had been changed to Metoclopramide Hydrochloride Monohydrate in Supplement 9.4. Members endorsed the recommendation that the change in title should be reflected in the BP. The Definitions in the associated formulation monographs (Metoclopramide Injection, Oral Solution and Tablets) would also be updated accordingly in the next edition of the BP.

British Approved Names As a consequence of additions to the Ph Eur, the following change would be made in a future BAN publication: Tacrolimus Monohydrate would be added as a new British Approved Name (Modified) to the entry for Tacrolimus.

179 **British Pharmacopoeia 2019: Text Review Dates** COM(17)39

BP 2019 Text Review Dates Dates for reviewing the BP 2019 text using the document review tool (DRT) had been agreed and were provided for information.

BP Editorial Style Guide The BP Style Guide provided guidance on drafting monographs and was only intended for internal use. The individual chapters had recently been reviewed and the Secretariat would provide a single document containing all the individual chapters to coincide with the first batch of text for review.

BP Policy List The Secretariat was in the process of expanding the draft policy list that had been presented at the July meeting. This would be available to coincide with the first batch of text for review.

Aide Memoire The Aide Memoire had been updated as agreed at the last meeting and a copy was provided for information.

V ANALYTICAL ISSUES

180 Assay Procedures: Use of 20 Tablets (or Capsules) COM(17)40

Background For Assays in solid oral dosage form monographs the usual approach was to carry out the procedure on the powder obtained after "weighing and powdering 20 tablets" or on the "mixed contents of 20 capsules". The rationale behind this approach was to ensure that the results were obtained on a representative batch. In some instances, however, the use of whole tablets or capsules was specified.

Whole unit methods versus ground samples At the recent meeting of EAG MC3: Medicinal Chemicals, the Laboratory had reported results obtained on a product that had shown low recovery of the active ingredient using a ground sample but good recovery when whole units were used.

The group had discussed the use of use of whole tablet/capsule methods and the traditional BP approach of using ground samples. There was now a greater use of whole unit methods over ground sample methods due to a variety of reasons including (1) a lack of sufficient fume cupboards to grind samples manually, (2) difficulties in obtaining a uniform fine sample for some products and (3) degradation caused by the heat from electronic grinders.

Members were reluctant to change the current preferred approach but agreed that where a manufacturer had provided a validated method using whole tablets or capsules, this should be included in the BP. It was noted that companies could use their own methods in routine testing providing these were validated against the official pharmacopoeial method.

Permitted changes and additional information EAG MC3 had questioned whether manufacturers could routinely use whole unit methods in routine testing when the official BP method specified the use of a ground sample. The Secretariat had confirmed that this would be permitted under the statement in the General Notice on Assays and Tests relating to the use of alternative methods. Members confirmed that the current provisions were sufficient and that there was no need to add anything further.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

181 Expert Advisory Groups, Panels of Experts and Working Parties COM(17)41

Expert Advisory Group HCM: Herbal and Complementary Medicines Members endorsed the recommendation to appoint Dr Anthony Booker (senior lecturer in Chinese Medicine and Medicinal Plant Science, University of Westminster) to EAG HCM.

Members endorsed the recommendation to appoint Professor Adrian Slater (Professor of Biomolecular Technology, De Montfort University) to EAG HCM. Professor Slater was Chair of Panel DNA: Identification Techniques and his appointment would facilitate a closer integration and understanding between the two groups, which were closely linked.

Expert Advisory Group MC2: Medicinal Chemicals Members endorsed the recommendation to appoint Dr Andrea Ruggiero (Associate Director of Pharmaceutical Services & CMC Regulatory Intelligence, Merck Serono) to EAG MC2.

Expert Advisory Group MC3: Medicinal Chemicals Mr V'Iain Fenton-May had retired as both Chair and member of EAG MC3 having served as its Chair for 10 years. He had attended his last meeting in September when the Secretariat and members had thanked him and paid tribute to his long service.

Members endorsed the recommendation to appoint Professor Matthew Almond, the current Vice-Chair, as Chair of EAG MC3 with immediate effect.

Retired members Mr Colin Cable had resigned from Panel CX: Excipients due to ill health and a letter of thanks had been sent. Mr Anthony James had recently resigned from EAG MC1 as he was no longer able to devote sufficient time to the work of the group due to changes in his responsibilities. Replacement members would be identified in due course.

MHRA Representatives A number of changes to MHRA representatives had recently been made and these were endorsed by members.

182 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(17)42

The report of the EAG BIO meeting (07:11:16) was approved. A lot of the discussions had been on issues relating to the MHRA Strategy document.

183 **Expert Advisory Group ULM: Unlicensed Medicines** COM(17)43

The report of the EAG ULM meeting (25:04:17) was approved and the following points were raised.

Nadolol Oral Suspension; Nifedipine Oral Suspension A member of EAG ULM had arranged for MSc students to carry out practical evaluation of the draft monographs.

Co-proxamol Tablets Concerns had been raised at a previous BPC meeting over the continued inclusion of the monograph for Co-proxamol Tablets in the BP. Members of EAG ULM had confirmed that the product was still widely used in the UK and had been strongly of the opinion that the monograph should be retained until such time that the formulation was no longer required.

184 **Expert Advisory Group MC1: Medicinal Chemicals** COM(17)44

The report of the EAG MC1 meeting (15:06:17) was approved and the following point was raised.

Primidone Tablets & Oral Suspension; Phenytoin Preparations As category 1 anti-epileptics, the monographs included non-interchangeability statements. The EAG had considered that inclusion of a dissolution test in the solid oral dosage form monographs might therefore be inappropriate and that a production statement approach might be suitable. It had been agreed to refer the matter to the Expert Advisory Group on Pharmacy before a decision was taken.

185 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(17)45

The report of the EAG HCM meeting (22:06:17) was approved. Professor Slater (Chair of Panel DNA) had attended the meeting which had been invaluable to the group when issues relating to DNA barcoding had been addressed. There had been an issue due to lack of standards to support draft monographs and steps would be taken to try and source these earlier during the monograph development process.

186 **Panel DNA: Identification Techniques** COM(17)46

The report of the Panel DNA meeting (19:07:17) was approved and the following points were raised.

Glehnia Littoralis Root It had been found possible to distinguish between Glehnia Littoralis and Adenophora (adulterant) and members endorsed the Panel's recommendation to elaborate a monograph for Adenophora.

Journal article Members had previously recommended publicising the innovative work of Panel DNA and an article entitled "DNA Barcoding for Industrial Quality Assurance" had recently been published in *Planta Medica.*

187 **Expert Advisory Group ABS: Antibiotics** COM(17)47

The report of the EAG ABS meeting (21:09:17) was approved and the following points were raised.

Amikacin Injection In light of the general difficulties experienced with HPLC methods using pulsed amperometric detection (PAD), and the increasing use of PAD methods, members of the group had considered it important for the BP Laboratory to develop expertise in this technique.

Colistimethate Preparations The Secretariat had highlighted a potential anomaly between the BP policy on Inhaled Products relating to Powders for Nebuliser Solutions and the General Monograph for Preparations for Inhalation and this would be drawn to the attention of EAG PCY.

Cefoxitin Injection Members endorsed the EAGs recommendation to amend the monograph in the BP 2019 and then to omit it from a future edition of the BP, pending the usual consultation procedure.

VII EUROPEAN PHARMACOPOEIA

188 **European Pharmacopoeia Update** COM(17)48

European Pharmacopoeia Commission

158th Session The draft report of the 158th Session of the EP Commission (June 2017) was available on the forum section of the BP website.

159th Session The 159th Session of the EP Commission would be held on 21st and 22nd November.

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UK Experts The list of UK members appointed to Ph Eur Expert Groups and Working Parties since 1st January 2017 was provided for information.

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. This included a list of items proposed for inclusion in the pan-European Paediatric Formulary.

VIII INTERNATIONAL COLLABORATION

189 **International Update** COM(17)49

Members were provided with an update on international activities.

8th International Meeting of World Pharmacopoeias Mr Pound and Dr Gardiner had attended the 8th International Meeting of World Pharmacopoeias, which had been held in Brazil in July. The draft technical annexes to the Good Pharmacopoeial Practices guidance document on Monographs for Compounded Preparations and Herbal Medicines had been discussed and were nearing completion. The results of a stakeholder survey regarding awareness and use of the document had been discussed, together with potential topics for future meetings.

The meeting had been followed by the 9th Annual Meeting of the Brazilian Pharmacopoeia at which a number of bilateral meetings had been held with representatives from the Indian, Brazilian and Vietnamese Pharmacopoeias to discuss areas of collaboration.

Joint Compendial Industry Group (BP/USP) Mr Young and Dr Radi had participated at this meeting with US industry groups by teleconference. The BP had provided an update on the BP, the consultations on Biologicals and Dissolution and the BP Customer Insight survey. Positive feedback had been received and the BP would continue to participate in future discussions.

World Health Organization Mr Evans had attended the 65th Consultation on International Non-proprietary Names (INN). A total of 109 new names had been discussed (of which nearly half were for biological substances) and 52 outstanding names. Mr Evans had given a presentation on the BP and British Approved Names.

Ms Corns had attended the WHO Expert Committee on Specifications for Pharmaceutical Preparations. The meeting had covered a wide range of activities including monographs for the International Pharmacopoeia (IP), general policies and Good Pharmacopoeial Practices.

China Inward Meeting The MHRA had hosted a delegation from China, including representatives from the Chinese Pharmacopoeia, the Chinese State Food and Drug Administration and the National Institute for Food and Drug Control who had been on a fact-finding visit to the UK. Mr Evans had attended the meeting and had given a presentation on the BP. There had been particular interest expressed in the BP, NIBSC and the Inspectorate and in the regulation of medical devices.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

190 PDA Conference

Mr Pound and Mr Gibb would be attending the Parenteral Drug Association Conference on Pharmacopoeias which would be held in Vienna during 2018.

191 Accommodation

The move to Canary Wharf was likely to take place in spring/early summer of 2018.

192 Work of the BP

Following discussion at the Corporate Executive Team, the BP had been asked to present a paper outlining the work of the BP to the MHRA Agency Board.

X ANY OTHER BUSINESS

193 Date of next meeting

Monday 5th March 2018.