SUMMARY MINUTES

of the

BRITISH PHARMACOPOEIA COMMISSION

A meeting of the British Pharmacopoeia Commission was held at 10 South Colonnade, Canary Wharf, London E14 4PU on Tuesday 12th March 2019.

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 M G Lee, Mr R Lowe, Professor J Miller, Ms S Palser (*lay member*) and Dr R Torano.

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

Apologies for absence were received from Professor M Simmonds and Dr P Varley.

Also present: Ms H Ashraf, Ms N Clothier, Ms H Corns, Mr P Crowley, Mr A Evans, Mr A Gibb, Ms S Gomersal, Mr H Makwana, Mr S Maddocks (*am only*), Mr M Whaley (*am only*) and Mr S Young. Mr I King (Policy Division), Ms E Razzano (Licensing) and Mr D Deutsch (Licensing) attended the meeting for the items recorded under minutes 276, 279 and 293 respectively.

273 **Introductory Remarks**

Welcome The Chair welcomed members to the meeting. He also welcomed Ms Hina Ashraf who had recently joined the Secretariat and was attending her first meeting.

Staff Ms May-Louise Wall and Dr Catherine Lenihan had recently left the Secretariat and Dr Alice Gardiner would shortly be transferring within the MHRA. Dr Gary Kemp had been temporarily promoted to the post of Publications Manager.

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.

I MINUTES

274 The minutes of the meeting held on 12th November 2018 were confirmed.

II MATTERS ARISING FROM THE MINUTES

275 The following matters arising from the meeting held on 12th November 2018 were noted.

Minute 249 – Dissolution Testing in the BP: Update The response to the BP consultation had been published on the BP website in February.

Minute 262 – Expert Advisory Group MC2: Medicinal Chemicals Professor Davidson had submitted proposals relating to several issues raised within the April 2018 MC2 Minutes and the intention was to include these items on the agenda for the July meeting.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

276 **Brexit**

An update on how the MHRA was preparing to deal with the outcome of the UK decision to leave the European Union was provided.

277 **Update from the Secretary and Scientific Director: Operational Transformation**

Mr Pound provided an update on activities associated with the Medicines and Healthcare products Regulatory Agency's Operational Transformation programme.

OPERATIONAL

278 **Innovation Board: Update** COM(19)1

An update on the activities of the Innovation Board was provided for information.

Background The joint BP-TSO Innovation Board had been established in August 2018 with the aim of providing improvements to the BP brand through a combination of increased revenue, customer satisfaction or increased efficiencies.

User Research A company had been commissioned to carry out an extensive review of BP users, including finding out who uses the BP products, together with how and why they use them. The research would also be used to identify areas for improvement to help meet the needs of current and future users.

Innovation Board Outputs A number of proposals had already been approved by the Innovation Board, including improvements to the website registration page to capture additional information on users and the inclusion of CAS Registry numbers in the BPCRS catalogue.

BP User Guide A guide on how to use the BP had been prepared and would shortly be included on the website. The guide provided general information on BP requirements, on navigating through the whole publication and on how to interpret the various parts of a monograph.

Track-changed monographs Following requests to highlight changes in revised monographs the Secretariat had considered a number of options to indicate such changes. In view of the complexity of the project it was expected that a simple system would first be introduced with the possibility of including additional features as the project progressed.

279 **AQbD Project Update** COM(19)2

Introduction Members were provided with an update on the Analytical Quality by Design (AQbD) feasibility study, which had been initiated in 2012. The project aimed to identify whether Quality by Design concepts could be used to produce more robust and rugged monographs, thereby potentially reducing the need for revisions due to analytical deficiencies. The BP/MHRA feasibility study was unique in its practical evaluation of the concept and the involvement of Licensing and Inspectorate colleagues.

Impact on Monograph Development The project had identified the differences in approach for companies developing methods to control specific products and

pharmacopoeias which provided methods that were suitable for a range of products. The Working Party had identified critical method parameters using various statistical tools of analysis, such as the “fishbone diagram” and “Failure Mode Effect Analysis”. A multi-factor approach had been adopted which had allowed the analysis of several factors at the same time and provided a better understanding of how these factors individually and cumulatively affected the performance of the method. It also reduced the number of samples for analysis to a realistic and representative amount, whilst still providing a high level of assurance that the eventual method chosen would be suitable for all formulations.

Impact on Monograph Description The Working Party had considered how best to include AQbD concepts within a monograph and several approaches had been proposed.

Stakeholder Engagement Consultation with stakeholders regarding the implications of applying AQbD principles to BP monographs would be carried out. It was intended to launch the consultation in May, with a view to providing feedback to Commission at the November meeting.

280 **British Pharmacopoeia Laboratory** COM(19)3

British Pharmacopoeia Laboratory Reports The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the November 2018 meeting was provided for information.

British Pharmacopoeia Chemical Reference Substances Tables providing information on BPCRS up to the end of January 2019 were provided for information.

IV FUTURE PUBLICATIONS

281 **British Pharmacopoeia 2020 Publications** COM(19)4

BP 2020 The Secretariat was currently preparing text for inclusion in the British Pharmacopoeia 2020 and the British Pharmacopoeia (Veterinary) 2020. All items included in the 9th Edition of the European Pharmacopoeia, together with those from Supplements 9.1 to 9.8, would be incorporated in either the BP 2020 or the BP (Vet) 2020, as appropriate. The 2020 publications would be published in August and would come into effect on 1st January 2020.

Electronic updates The text from Supplement 9.6 to the Ph Eur 9th Edition had been added to the online BP in December 2018, in advance of its implementation on 1st January 2019. The text from Supplements 9.7 and 9.8 would be available in advance of their implementation dates on 1st April and 1st July 2019 respectively.

Text for approval The first batch of new and technically revised monographs for the BP 2020 publications had been reviewed by members during February. The final batch of text would be posted on the Document Review Tool (DRT) on **5th April**, with a deadline for comment of **23rd April**.

Preliminaries Members recommended that the British Pharmacopoeia 2020 and the British Pharmacopoeia (Veterinary) 2020 should be published and confirmed that the draft Prefaces to both publications were acceptable.

Technical/Editorial Changes In addition to the changes arising through EAG discussions, the following changes would also be made in the BP 2020: (i) with the exception of those monographs that would be revised in either the BP 2021 or the BP 2022, the title of monographs containing split standard terms would be updated as previously agreed;

(ii) minor editorial changes would be made to the opening statements of all monographs for unlicensed formulations.

282 **Monographs for Omission from the BP 2020 and BP (Vet) 2020** COM(19)5

BP 2020; BP (Vet) 2020 Since publication of the BP 2019 publications, a number of monographs had been identified as candidates for omission from the BP 2020 publications.

In accordance with usual practice, the Secretariat would contact countries in which the BP was used to ascertain if the products were still available/used before finalising the list and the list would be included on the BP website for public comment. Members endorsed the recommendation to omit the identified monographs from the BP 2020 and the BP (Vet) 2020, subject to any comments received. In accordance with regulation 252 (2c) of the Human Medicines Regulations 2012, these monographs would continue to remain in force.

Review; Guiding Principles Several monographs were usually omitted from new editions of the BP and the BP (Vet). These were generally identified through the day to day work of the Expert Advisory Groups, as the Secretariat became aware of items that were no longer licensed and as a consequence of suppression of Ph Eur monographs. The monographs for omission were currently identified on an *ad-hoc* basis, there was no formal review process.

It was intended to carry out a systematic review of the whole monograph portfolio. Several EAGs had already carried out a review of certain of their monographs.The intention was for this review to be applied more widely in the future and a series of draft principles had been developed to help guide decisions and ensure a consistent approach is taken across the various EAGs.

Members supported the development of a set of principles on which to base future decisions.

283 **Approved Synonyms** COM(19)6

New monographs The proposed new Approved Synonyms relating to items added to the European Pharmacopoeia by means of Supplements 9.7 and 9.8 to the 9th Edition were approved. The items would be added to Appendices XXI B and XXI B (Vet) by means of the BP 2020 and would be incorporated within the online updates to the BP 2019 publications.

Title changes The titles of eight monographs had been changed in Supplements 9.7 and 9.8, mostly to indicate the degree of hydration, and these changes would be reflected in the BP 2020. In accordance with established policy the former titles would be retained as subsidiary titles, which had the same legal weight as the main title, and the definitions of relevant formulation monographs would be amended to reflect the new titles.

British Approved Names As a consequence of additions to the Ph Eur, the following changes would be made in a future BAN publication: Esomeprazole Sodium and Nilotinib Hydrochloride would be added as new BAN (Modified) to the entries for Esomeprazole and Nilotinib respectively.

284 **British Approved Names 2017: Supplement No. 3** COM(19)7

Supplement No. 3 to British Approved Names 2017, containing 35 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 text and to send any comments to the Secretariat by **26th March**.

Liposomal products The draft Supplement included three modified entries relating to liposomal forms of Amphotericin, Daunorubicin and Doxorbubicin. Members were informed that products prepared using active pharmaceutical ingredients encapsulated with liposomes released the drug substance over a longer time than conventional-release formulations of the same strength. This could lead to a patient receiving a fatal dose of a particular drug if the wrong formulation was administered. This matter had been discussed at the recent EAG NOM meeting when it had been agreed that distinctive names for liposomal and non-liposomal forms were required to distinguish between the two forms. Members endorsed the recommendations to add the following BANM in the Supplement: Liposomal Amphotericin B; Liposomal Daunorubicin Hydrochloride; Liposomal Doxorubicin Hydrochloride; Pegylated Liposomal Doxorubicin Hydrochloride.

285 **Monograph Initiation: Candidate Monographs** COM(19)8

EAG Recommendations A number of monographs had been identified for addition to the BP work programme through routine EAG activities. These related to formulations associated with new Ph Eur drug substance monographs or to potential family monographs. Members endorsed the addition of the identified items to the work programme.

2017 PCA Prescribing Data The Secretariat had examined the 500 most prescribed items in the 2017 Prescription Cost Analysis data prepared by NHS Digital. A number of items had been identified as potential candidate monographs and it was agreed that these should all be added to the work programme.

Candidate drug substance monographs A number of drug substances had been identified for which over 500,000 items had been prescribed, but which were not the subject of a current monograph and were not included on the Ph Eur work programme. It was agreed that the Secretariat should first contact manufacturers to ascertain if they would be willing to provide data to support development of a Ph Eur monograph before any requests for additions to the work programme were submitted.

V ANALYTICAL ISSUES

NONE.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

286 **Expert Advisory Groups, Panels of Experts and Working Parties** COM(19)9

Following the membership review, letters of invitation had been sent to all new and re-appointed members and letters of thanks had been sent to those who had retired from the various Expert Advisory Groups and Panels of Experts.

Expert Advisory Group ABS: Antibiotics There had been an outstanding vacancy on EAG ABS for a member with expertise in the field of veterinary medicine. Dr Gillian Clarke (Acting Head of Pharmaceuticals, Veterinary Medicines Directorate) had been identified as a suitable candidate member and she had attended the recent meeting of EAG ABS as an invited expert. The appointment was supported by the Chair and Vice-Chair of EAG ABS

and further justification had been provided in the meeting papers. Members endorsed the appointment of Dr Clarke to EAG ABS.

Working Party AQbD: Analytical Quality by Design The need for additional expertise on the Working Party had been identified and Dr Phil Borman (Director of QbD Development for Small Molecules, GlaxoSmithKline) had been proposed as a suitable member. His appointment was supported by the Chair of WP AQbD and justification had been provided. Members endorsed the appointment of Dr Borman to WP AQbD.

287 **Expert Advisory Group ABS: Antibiotics** COM(19)10

The report of the EAG ABS meeting (27:9:18) was approved.

288 **Expert Advisory Group MC3: Medicinal Chemicals** COM(19)11

The report of the EAG MC3 meeting (8:10:18) was approved and the following points were raised.

Amitriptyline Preparations; Related substances It was noted that the approach for naming impurities should be in accordance with recommendations in the Style Guide.

Rotigotine Transdermal Patches; Uniformity of content It was questioned whether a method which included a symmetry factor requirement of "between 0.8 and 2.8" was suitable. The Laboratory would be asked to confirm the suitability of the requirements during the work to establish the corresponding BPCRS.

289 **Expert Advisory Group ULM: Unlicensed Medicines** COM(19)12

The report of the EAG ULM meeting (15:10:18) was approved and the following points were raised.

Sterility of Extemporaneous Preparations The General Monograph on Unlicensed Medicines would be amended in the BP 2020 to reflect that alternative approaches to the sterility test might be required since it would be impossible to carry out the pharmacopoeial test on extemporaneously prepared preparations which were available in limited amounts.

University Collaboration; Validation of Analytical Procedures Further work was being undertaken by students with a view to supporting monograph development and the Secretariat had provided some guidance to assist with future projects.

290 **Expert Advisory Group MC2: Medicinal Chemicals** COM(19)13

The report of the EAG MC2 meeting (24:10:18) was approved and the following points were raised.

Clenbuterol Oral Solution An identification test using a liquid chromatographic method with UV-Diode Array Detection had been proposed and accepted. Methods using LC/UV-DAD had not yet been included within the BP but were under discussion by the *ad-hoc* group on New Analytical Technologies.

291 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(19)14

The report of the EAG HCM meeting (22:11:18) was approved and the following points were raised.

Herbal Photographs The EAG had agreed that it would be useful to include photographs illustrating characteristic microscopic and macroscopic features of herbal materials in a future publication.

Cannabis The current position was that there was no immediate requirement to develop a national monograph for Cannabis (either the herbal material or products).

292 **Expert Advisory Group MC1: Medicinal Chemicals** COM(19)15

The report of the EAG MC1 meeting (5:12:18) was approved and the following point was raised.

Busulfan Preparations The Laboratory no longer had an electron capture detector, which was specified in the current monograph for Busulfan Tablets and a number of other monographs. However, it was noted that the Laboratory could use the detector owned by the MHRA Laboratory if testing was required.

VII EUROPEAN PHARMACOPOEIA

293 **European Pharmacopoeia Update** COM(19)16

European Pharmacopoeia Commission The draft report of the 162nd Session of the EP Commission (November 2018) was available on the forum section of the BP website. The 163rd Session would be held between 19th and 20th March.

Members discussed items from the 162nd Session and items for the forthcoming March Session and advised the UK delegation accordingly.

10th Edition of the European Pharmacopoeia An international conference had been organised by the EDQM to celebrate the forthcoming publication of the 10th Edition of the European Pharmacopoeia and the 25th anniversary of the establishment of the OMCL network and the Certification procedure.

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

294 **International Update** COM(19)17

Members were provided with an update on international activities.

United States Pharmacopeia A teleconference had been held in February to discuss: future monograph collaborations; progress on the Memorandum of Understanding (MOU) between the two organisations; future issues for consideration at the International Meetings of World Pharmacopoeias. The MOU was now ready to be signed by both parties.

Commonwealth Standards Network (CSN) Mr Pound and Mr Evans had participated in a teleconference in January with representatives from the British Standards Institution (BSI) to discuss the BSI project to increase the understanding and provision of standards within Commonwealth countries. The BP/MHRA had been invited to liaise with BSI to include medicinal standards required within the UK on their website in order to generate a wider understanding.

Chinese National Medical Products Administration (NMPA) A delegation from the MHRA, including Dr Samantha Atkinson, had attended the NMPA Symposium in Beijing in November 2018. This had included a break out session on pharmacopoeias and discussions on potential collaborations between the BP/MHRA and the Chinese Pharmacopoeia.

10th International Meeting of World Pharmacopoeias Mr Pound and Mr Gibb had attended the 10th IMWP meeting in March, held in Geneva. The main topic of discussion had been the draft White Paper on the Value of Pharmacopoeial Standards, which focussed on the contribution of such standards to the protection of public health and was aimed at all stakeholders across the globe.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

See under minute 277.

X ANY OTHER BUSINESS

295 BPC Appraisals

Annual appraisals for members of the BP Commission would be carried out in May.

296 Date of next meeting

Monday 1st July 2019.

FOR INFORMATION:

297 Items for Future Meetings

An updated list of items for discussion at future meetings was provided for information. It was agreed that an entry for annual updates to the BP work programme should be added to the list. Further updated lists would be provided at future meetings.