**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 Monday 9th July 2018.

**Present:** Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Dr J Beaman, Dr A M Brady, Dr A Coulson, Dr A Gleadle (*lay member*), Dr M G Lee, Mr R 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.

Apologies for absence were received from Professor M Almond and Dr G Cook.

Also present: Mr P Crowley, Mr L Elanganathan, Mr A Evans, Mr A Gibb, Ms S Gomersal, Dr G Kemp, Ms C Lockie-Williams, Mr S Maddocks, Mr H Makwana, Mr M Whaley and Mr S Young.

Dr A Gardiner attended the meeting for the item recorded under Minute 230. Mr Adrian Bartlett attended the meeting for the item recorded under Minute 226.

225 **Introductory Remarks**

**Welcome** The Chair welcomed members to the first meeting in the new building.

**Staff** This was the last meeting for Mr Elanganathan who would shortly be leaving the Secretariat to join the Inspection Action Group within the Inspection, Enforcement and Standards Division. The Chair thanked Mr Elanganathan for his contribution to the BP over the last 18 months.

**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.

226 **Brexit**

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

**I MINUTES**

227 The minutes of the meeting held on 5th March 2018 were confirmed.

**II MATTERS ARISING FROM THE MINUTES**

228 The following matters arising from the meeting held on 5th March 2018 were noted.

**Minute 199 – Performance and Class-based Standards: BP Working Party** The proposed terms of reference and membership of the new BP Working Party on Alternative

Approaches for Documentary and Physical Standards for Biotechnological Products (BIO-DPS) had been endorsed by members by correspondence in May.

**Minute 201 – BPC Sponsors** Dr Gleadle had agreed to act as sponsor for the BP Transformation programme.

**Minute 203 – Alkylsulfonate Esters: Production Statements in BP Monographs** A revised form of words had been agreed after the last meeting and had been agreed by EAG MC1 at their meeting held on 15th June 2018.

**Expert Advisory Groups, Panels of Experts and Working Parties** Mr Jasbinder Sumal and Dr Mark Carine had accepted the invitations to join EAG ABS and Panel DNA respectively. Since the last meeting Dr Darren Edwards had resigned from EAG MC2.

## III REPORTS AND CORRESPONDENCE

***GOVERNANCE***

229 **British Pharmacopoeia Transformation: Update** COM(18)24

An update of the work related to the BP Transformation programme was provided.

230 **MHRA Strategy for Pharmacopoeial Quality Standards for Biological Medicines: Update** COM(18)25

A summary of the recent activities was provided for information, together with a copy of the official MHRA response to the consultation. The document included a Strategic Work Programme which identified the key activities for the Agency: (i) Standards development; (ii) Engaging with users and building knowledge; (iii) Our international peers.

**Standards development** There were a number of different areas within this overall activity with which the BP was heavily involved.

***Alternative approaches*** The Agency had agreed to the establishment of a BP Working Party (WP BIO-DPS) with the remit of exploring the potential value of performance and class-based standards in enabling and supporting innovation through a flexible approach.

***Advanced Therapy Medicinal Products (ATMPs)*** The value of BP and NIBSC standards for ATMPs had been highlighted in the Medicines Manufacturing Industry Partnership's Advanced Therapies Manufacturing Action Plan and in the response to the MHRA Consultation. The intention was to establish a further Working Party to provide recommendations for standards in this area.

***Raw Materials*** Standards for raw materials had been identified as an "unmet need" but further work was required to understand the scope of this work.

**WP BIO-DPS: Alternative Approaches for Documentary and Physical Standards for Biotechnological Products** The Commission had approved the membership and terms of reference for the Working Party by correspondence (COM(18)23 refers) and the first meeting of the group had been held in May.

***OPERATIONAL***

231 **Dissolution Testing in the BP: Update** COM(18)26

**Introduction** A number of issues had been discussed at previous meetings regarding the current approach to dissolution testing. A public consultation entitled "*Dissolution testing in BP finished product monographs for solid oral dosage forms*" had been run between January and April 2017 with the aim of defining future policy on this issue. The responses had been considered at a workshop held during the EAG Pharmacy meeting held in September 2017. Following this meeting the Secretariat had prepared a draft public response which was intended to help outline the future approach to dissolution testing and this had been discussed at the February 2018 PCY meeting. An updated version of the draft response was provided for discussion.

**Discussion** Members endorsed the content of the response document.

It was agreed that the response document should be disseminated to the public by inclusion on the BP website. Other avenues would also be explored to ensure that the outcome and intentions reached as wide an audience as possible. The PCY Secretariat would work closely with the other EAGs to ensure that a consistent approach to revising monographs was taken. It was intended that updates would be provided to the relevant EAGs at the autumn meetings.

**Appendix II B** The current Appendix on Dissolution was split into various sections, including points specifically relating to BP monographs and non-mandatory Ph Eur information. It had been accepted that the current layout could be confusing to users. The Secretariat had agreed to re-order the information in a more logical order for inclusion in a future publication with a view to presentation of proposals at the November meeting.

**Supplementary Chapter I E** The current Supplementary Chapter on Dissolution Testing included a schematic diagram indicating which acceptance criteria should be applied when the limits were not included in the individual monographs. The Secretariat had agreed to simplify the diagram for clarity.

232 **Extemporaneous Preparations** COM(18)27

**Background** At the July 2016 meeting it had been agreed that, following a public consultation on monographs containing extemporaneous preparation details, such information should be removed from relevant monographs and included in a new Supplementary Chapter. It had been accepted that there may be instances where the information would need to be retained within the monograph and that where, historically, a fixed strength had been included this should be retained. The Expert Advisory Groups on Pharmacy (PCY) and Unlicensed Medicines (ULM) had discussed this issue at subsequent meetings in order to develop a consistent approach to reviewing and updating the affected monographs. This had resulted in the development of a decision tree which provided clear guidance as to whether the extemporaneous preparation details should be retained in a monograph or moved to a Supplementary Chapter and which had been accepted by both EAGs PCY and ULM.

Members endorsed the proposed course of action outlined in the decision tree.

**Supplementary Chapter** It was noted that both licensed and unlicensed formulations were expected to be identified in the review. Members endorsed the recommendation to develop a new Supplementary Chapter that would incorporate the existing information that

was currently included in SC V E, which included examples of well-established formulae and/or methods of preparation for a number of unlicensed formulations.

233 **Analytical Quality by Design Project Update** COM(18)28

Members were provided with an update on the 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 reducing the need for revisions and allowing the adoption of innovative analytical techniques.

**Global Perspective** The International Council for Harmonization (ICH, previously known as the International Conference on Harmonization) was developing a guideline on Lifecycle Management (Q12) which included several QbD concepts associated with quality-risk management and was currently out for public consultation. The USP Convention had published several stimuli articles addressing QbD principles, together with proposals for a new USP General Chapter. Dr Kemp would be providing an update on the BP feasibility study at a USP workshop later in the year.

**Project update** An HPLC Assay method had been chosen as the case study for applying AQbD concepts to pharmacopoeial analysis for a widely used product available from a number of manufacturers. Laboratory work had been undertaken and the results had been analysed using statistical software tools. The proposed method had been shown to be robust with respect to minor variations in the chromatographic conditions.

A sub-group of the AQbD Working Party had been established in order to investigate the concept of Analytical Target Profiles (ATP), that is a predefined objective that stipulates the performance requirements for the analytical procedure. The sub-group would be making recommendations to the Working Party later in the year and these would be drawn to the attention of Commission at a future meeting.

234 **British Pharmacopoeia Laboratory** COM(18)29

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

**British Pharmacopoeia Chemical Reference Substances** Tables providing information on BPCRS up to the end of May 2018 were provided for information. The Laboratory was on target to ensure that the 15 new BPCRS required to support the new and revised monographs in the BP 2019 would be available by 1st August, which was well in advance of the implementation date.

**Out of stock BPCRS** In response to a request at the last meeting, information on out of stock items and their expected date for availability had also been provided. This also highlighted those BPCRS for which it had not been possible to obtain material for testing. Monthly updates relating to BPCRS that had been released, and those that were out of stock, were included on the BP website.

## IV FUTURE PUBLICATIONS

235 **Consistency in Powders for Oral Liquid Monographs** COM(18)30

**Format** The current policy regarding monographs for Oral Solutions and Oral Suspensions that are presented as dry powders was to test the reconstituted solution or suspension and to include assay limits relating to the freshly constituted formulation and at the end of the

period of use. The title was in the form “[XXXX] Oral Solution/Suspension”, the dry ingredients were required to comply with the requirements for Powders and Granules for Oral Solutions and Oral Suspensions and the constituted preparation was required to comply with the requirements for Oral Liquids.

**Stand-alone Monographs** The current approach for monographs for injections or infusions presented as dry powders was to prepare separate monographs for the “Injection/Infusion” and for the “Powder for Injection/Infusion” if both presentations were commercially available and it had been questioned whether a similar approach for Oral Liquids should be adopted. It was understood that for those items that were the subject of a monograph the formulations were only available as dry powders. It was therefore agreed that the current approach should be retained and that stand-alone monographs were not required. As the patient received the liquid form, it was appropriate that the monograph tests related to the constituted liquid.

**Template** A draft template had been prepared which reflected the current agreed wording for Oral Solutions/Suspensions presented as dry powders. The text was agreed, subject to minor editorial corrections.

236 **Monograph Definition Statements: Excipients** COM(18)31

Monographs for injections or infusions presented as dry powders defined the formulation as “a sterile material consisting of [XXXX] with or without excipients”. This approach was intended to ensure that the monograph did not place any restrictions on the formulation in terms of excipients or method of manufacture and had been followed for many years. The current approach had recently been questioned by the Expert Advisory Group on Antibiotics in view of concerns over the suitability of monograph methods that had been developed for products that did not contain excipients to those that did contain excipients.

It was noted that as newer products became available the formulations could change significantly from that of the original product. Similarly, it was not possible for a BP monograph to cover formulations that might become available in the future and the onus was on a manufacturer to demonstrate that a new formulation complied with the requirements of a published monograph. As methods improved over time there was the chance to update monographs accordingly. This applied to all dosage form monographs, not just injections or infusions supplied as dry powders, and it was agreed that the current wording should remain unchanged.

## V ANALYTICAL ISSUES

NONE.

## VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

237 **Expert Advisory Groups: Membership Review** COM(18)32

The term of office for all members of the Expert Advisory Groups, Panels of Experts and Working Parties of the BP Commission would expire on 31st December 2018. A full membership review was being undertaken and the Secretariat would work closely with individual EAG/Panel/WP Chairs throughout the process.

**Current members** The various EAG Secretariats were in the process of identifying those members on their current groups that should be re-appointed or retired and to identify areas of expertise that needed to be filled.

**New members** The following steps had/would be taken to identify potential candidate members during the next few months: seeking input from current EAG and BPC members; inclusion of a note inviting expressions of interest on the BP website; alerting individuals and organisations directly regarding the opportunity to join an EAG/Panel/WP. Members were encouraged to promote the chance to join an EAG through their networks in order to generate as wide a range of potential new members as possible. All interested parties would be required to provide a CV and a supporting statement.

238 **Expert Advisory Group NOM: Nomenclature** COM(18)33

The report of the EAG NOM meeting (14:02:18) was approved. A significant part of the meeting had been taken up with discussing the draft content of Supplement No. 2 to British Approved Names 2017. The updated Supplement had been confirmed at the last meeting (minute 209 refers) and was now with the publisher. Members noted the contribution from Dr Gerry Moss regarding the chemical names.

239 **Expert Advisory Group PCY: Pharmacy** COM(18)34

The report of the EAG PCY meeting (22:02:18) was approved and the following points were raised.

**Dissolution (Anti-epileptic Drugs)** It had been noted that there were some inconsistencies in the category 1 anti-epileptic formulation monographs and steps would be taken to ensure a harmonised approach across the relevant EAGs.

**Nebuliser Products** EAG PCY had recommended that a request should be submitted to the EP Commission to revise the Ph Eur monograph for Preparations for Inhalation to include a section relating to Powders for Nebuliser Solutions. This request had not yet been sent.

240 **Expert Advisory Group ABS: Antibiotics** COM(18)35

The report of the EAG ABS meeting (27:02:18) was approved.

241 **Expert Advisory Group ULM: Unlicensed Medicines** COM(18)36

The report of the EAG ULM meeting (23:04:18) was approved and the following points were raised.

**Dispensing and Supply Statements** The EAG had supported the PCY/BPC recommendation to remove these statements from individual monographs, but had favoured retaining the information in a suitable location if feasible.

**Reconstituted Intravenous Preparations** It was intended to include additional information on these preparations in the Supplementary Chapter on Aseptic Preparation of Unlicensed Medicines and proposals would be submitted at a future meeting.

**Ferric Chloride Injection** A member questioned whether Specials and NHS manufacturers would have the necessary equipment to carry out the proposed Assay using ICP-OES. The sole supplier had provided validation data to support the method and it was noted that the technique was widely used.

**Parenteral Nutrition Solutions; Assay for Glucose** The need for a glucose assay was acknowledged, but to date a validated method had not been provided. The use of optical

rotation was suggested, although this would not be suitable for lipid-containing formulations.

There were many different PN formulations available and it had been difficult to develop a suitable monograph. Members affirmed the EAGs view that it was better to develop a monograph that provided some control over the major ingredients rather than not providing a standard. While noting the difficulties, however, the consensus was that steps should be taken to ensure that an assay for glucose should be included in the monograph, if possible.

## VII EUROPEAN PHARMACOPOEIA

### 242 European Pharmacopoeia Update COM(18)37

**European Pharmacopoeia Commission**: **160th and 161st Sessions** The draft report of the 160th Session of the EP Commission (March 2018) was available on the forum section of the BP website. The 161st Session had taken place in June and the report would be available in due course. Members discussed items from both sessions and from the forthcoming November session and advised the UK delegation accordingly.

**Homoeopathic Working Party** Following suspension of the Working Party, a meeting had been held in June to try and resolve the on-going differences between delegations. The EDQM had thanked the UK for helping to facilitate a way forward.

**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 and to the work programme of the Paediatric Formulary Working Party was presented for information.

## VIII INTERNATIONAL COLLABORATION

### 243 International Update COM(18)38

Members were provided with an update on international activities.

**International Meeting of World Pharmacopoeias** Mr Pound and Dr Kemp had attended the 9th International Meeting of World Pharmacopoeias which had been held in Vietnam. The following areas had been included on the agenda: Good Pharmacopoeial Practices; hot topics (including advances in technology and the establishment of reference materials); the replacement of microbiological methods of Assay by HPLC; collaborating models between pharmacopoeias; public and stakeholder engagement.

**United States Pharmacopeia** A meeting between the BP and the USP had been held in April to discuss current and future projects including: organisational changes; the development of a Memorandum of Understanding between the two parties; the biologicals consultation; AQbD; Brexit.

**WHO** Mr Evans and Dr Radi had attended the 66th International Non-proprietary Names Consultation in May during which proposals for 137 new names (including 84 biologicals) had been discussed. Mr Evans had been elected as Vice-Chair (Chemicals) for the meeting.

Ms Corns had attended the WHO Consultation on Screening Technology, Sampling and Specifications in May during which the monographs for Moxifloxacin Tablets and Pyrimethamine Tablets, which were being jointly developed by the BP and the International Pharmacopoeia, had been discussed.

**OMCL Network** Mr Young, Mr Whaley and Ms Li-Ship had attended the annual meeting of the EDQM Official Medicines Control Laboratories Network, held in Bosnia, at which the delegates exchanged information regarding testing and surveillance experiences and the co-ordination of future work. The next meeting of the network would be held in London in May 2019.

**NPA Meeting** Mr Young had attended the meeting of National Pharmacopoeial Authority Secretaries, held in Croatia. Discussion topics included the proposed adaptation procedure, dissolution, stalled monographs and ways to improve collaboration between NPAs and National Competent Authorities.

**DIA CMC Workshop (Basel)** Mr Pound and Dr Varley had attended the Drug Information Association workshop which had focussed on current challenging topics within the global pharmaceutical/biopharmaceutical arena. Mr Pound had given a presentation on "MHRA Perspectives on Pharmacopoeial Standards for Biological Medicines".

## IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

### 244 MHRA Activities

***Director of IE+S*** Members were pleased to note that Dr Samantha Atkinson, former Secretary and Scientific Director of the BP, had been appointed as the Director of the Inspection, Enforcement and Standards Division. On behalf of the Commission the Chair wished to place on record his thanks to Dr Atkinson for her contribution to the BP operation.

***Valsartan*** The recent recall of Valsartan-containing products, due to the presence of a potential carcinogenic impurity in the drug substance, was noted. Work was being undertaken to assess the need to undertake laboratory testing and/or to update the active substance and product monographs.

## X ANY OTHER BUSINESS

### 245 Items for Future Meetings COM(18)39

In response to previous requests to provide an indication of target meeting dates for outstanding policy items, a list of future agenda items had been provided for information.

### 246 Date of next meeting

Monday 12th November 2018.