SUMMARY MINUTES

of the

BRITISH PHARMACOPOEIA COMMISSION

A meeting of the British Pharmacopoeia Commission was held at NIBSC, Blanche Lane, South Mimms, Potters Bar, Herts EN6 3QG on Monday 12th November 2018.

Present: Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Dr A M Brady, Dr G Cook, 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 (*Secretary & Scientific Director*), Dr F J Swanson.

Apologies for absence were received from Professor M Almond and Dr J Beaman.

Also present: Ms N Clothier, Mr P Crowley, Mr A Evans, Dr A Gardiner, Mr A Gibb, Ms S Gomersal, Dr C Howard, Dr G Kemp, Mr H Makwana and Mr S Young. Mr Andrew Queen (MHRA) also attended the meeting.

247 **Introductory Remarks**

Welcome The Chair welcomed members to the meeting which was, exceptionally, being held at the offices of the National Institute of Biological Standards and Control. He offered a warm welcome to Dr Christian Schneider (Director of NIBSC), Dr Chris Burns (Head of Biotherapeutics, NIBSC) and Professor Jack Price (Head of Advanced Therapies, NIBSC) who attended the meeting for the item recorded under minute 252. He also welcomed Ms Naomi Clothier, the new BP fast streamer, and Mr Andrew Queen from the MHRA Communications Division.

Obituaries Members had been saddened to learn of the death of Dr Andrew Coulson during the summer. Dr Coulson had been an active member of the Commission since 2012 and had been the Vice-Chair of the Panel of Experts on Veterinary Medicines. The Commission observed a minutes silence in remembrance of Dr Coulson.

Members were also saddened to learn of the deaths of Dr Adrian Thomas, a long-standing member of the Expert Advisory Group on Biological and Biotechnological Products and a former member of EAG ABS: Antibiotics, and of Mr Peter Murray who had been a member of EAG MC2: Medicinal Chemicals for almost 10 years.

Members This was the last meeting for Dr Matthews, who had been a member of the BP Commission since 2010. The Chair paid tribute to Dr Matthews 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 member and Vice-Chair of the Expert Advisory Group on Pharmacy, as Chair of the Panel of Experts on Excipients and member of the Panel of Experts on Microbiology. Dr Matthews had shared his extensive knowledge both within and outside meetings and would be missed.

Staff Dr Krisztina Radi and Mr Laxsaan Elanganathan had both left the Secretariat in July. Mr James Pound had been made permanent Secretary and Scientific Director and Mr Alastair Gibb had been temporarily promoted to the post of Editor-in-Chief.

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

248 The minutes of the meeting held on 9th July 2018 were confirmed.

II MATTERS ARISING FROM THE MINUTES

249 The following matters arising from the meeting held on 9th July 2018 were noted.

Minute 231 – Dissolution Testing in the BP: Update This matter had been discussed at the recent EAG PCY: Pharmacy meeting. It was intended that the updated Appendix and Supplementary Chapter would be included in the BP 2020 and draft revised text would be provided for confirmation.

Minute 234 – British Pharmacopoeia Laboratory Interim updates providing information on BPCRS stock levels had been provided in August and October as agreed.

Minute 239 – EAG PCY Minutes: Nebuliser Products A request for revision of the Ph Eur monograph for Preparations for Inhalation had been submitted to the EP Commission.

Minute 241 – EAG ULM Minutes: Parenteral Nutrition Solutions Information had been sought on a suitable method to determine the Glucose content and the EAG was considering a number of options.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

250 Declaration of Interests: Annual Declaration

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.

251 Operational Transformation

An update on the Medicines and Healthcare products Regulatory Agency's Operational Transformation programme was provided.

252 Biological Standardisation COM(18)40

NIBSC Dr Schneider provided an introduction to the work carried out at NIBSC. The organisation had been in existence for nearly 100 years and had been part of the MHRA since 2013. NIBSC was the UK Official Medicines Control Laboratory and was a recognised world leader in biological standardisation.

Dr Burns gave an overview of the work of the Biotherapeutics Division which had a wide remit including albumin, cytokines, heparins, hormones and monoclonal antibodies.

Professor Price gave an overview of the work of the Advanced Therapies Division. This was the newest division in NIBSC and was responsible for the areas of Gene Therapy, Somatic Cell Therapy and Tissue Engineering.

The Chair thanked all the speakers for their presentations and for the opportunity to learn about the scope of the work at NIBSC. Mr Pound also thanked the speakers for the chance to hold the meeting at NIBSC and highlighted the importance of the strong links between the BP and NIBSC.

British Pharmacopoeia Mr Gibb provided a brief update on the MHRA strategy for pharmacopoeial standards for biological medicines. Members were reminded that there were three key areas of the strategy: (i) exploring alternative approaches to standards development, (ii) communication and engagement with users; (iii) engagement with international peers. The alternative approach to standards development was being addressed by the BIO-DPS Working Party.

253 **British Pharmacopoeia Transformation: Update** COM(18)41

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

254 **Brexit Update** COM(18)42

A brief update on issues affecting the MHRA was provided.

OPERATIONAL

255 **Expert Advisory Groups, Panels of Experts and Working Parties: Membership Review** COM(18)43

The term of office of all member of the Expert Advisory Groups, Panels of Experts and Working Parties would expire on 31st December 2018. The Secretariat had carried out a full review of membership over the last few months in close collaboration with the Chairs and Vice-Chairs of the relevant groups.

Review of current members The Secretariat and relevant Chairs had reviewed the composition of the current EAGs, Panels and Working Parties to identify those members that should be retained or retired.

Identification and review of proposed new members A note had been posted on the BP website between July and August inviting individuals who were keen to join one or more of the EAGs or Panels to submit a written expression of interest and a CV. The Commission and current EAG members were asked to raise awareness of the website invitation and a number of organisations were approached directly.

Proposals relating to each EAG, Panel and Working Party were discussed with the relevant Chairs and Vice-Chairs either by email, telephone or face to face discussion and the finalised proposals for each of the groups were presented.

Proposals The Chairs of the various groups were content with the process and the proposals relating to their specific groups. Commission endorsed the proposals relating to the membership of the following groups: Expert Advisory Groups ABS, BIO, HCM, MC1, MC2, MC3, NOM, PCY, ULM; Panels of Experts BLP, CX, DNA, IGC, MIC, RAD, VET, VIP; Working Party AQbD. The new terms of office would run from 1st January 2019 to 31st December 2022 and the Secretariat would shortly send out appropriate letters of invitation, re-appointment and thanks to new and existing members.

Working Party MCS: Microscopy Commission endorsed the recommendation to disband the Working Party. However, it was agreed that it might be useful to identify an appropriate expert in microscopy for EAG HCM in the future.

Working Party BIO-DPS: Alternative Approaches for Documentary and Physical Standards for Biotechnological Products; Ad-hoc Group NAT: New Analytical Technologies No changes to these groups were intended at this time.

256 **British Pharmacopoeia Laboratory** COM(18)44

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

British Pharmacopoeia Chemical Reference Substances Tables providing information on BPCRS up to the end of September 2018 were provided for information.

IV FUTURE PUBLICATIONS

257 **Approved Synonyms** COM(18)45

New monographs The proposed new Approved Synonyms relating to items added to the European Pharmacopoeia by means of Supplement 9.6 to the 9th Edition were approved. The items would be added to Appendix 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 title of the monograph for Benzathine Benzylpenicillin had been changed to Benzylpenicillin (Benzathine) Tetrahydrate in Supplement 9.6. Members endorsed the recommendation that the title in the BP should reflect the International Non-proprietary Name (Benzathine Benzylpenicillin Tetrahydrate), since this would be the name required for the label, and an approved synonym created.

The following title changes would be made in the BP 2020, together with any consequential changes to the associated formulation monographs: Calcifediol to Calcifediol Monohydrate; Lidocaine Hydrochloride to Lidocaine Hydrochloride Monohydrate. In accordance with established policy the former titles would be retained as subsidiary titles, which had the same legal weight as the main title.

British Approved Names As a consequence of additions to the Ph Eur, the following changes would be made in a future BAN publication: Imidacloprid would be added as a new British Approved Name; Sulfobutylbetadex Sodium would be added as a new BAN (Modified) to the entry for Betadex.

258 **British Pharmacopoeia 2020: Text Review Dates** COM(18)46

Dates for reviewing the BP 2020 and BP (Vet) 2020 text using the document review tool (DRT) had been agreed and were provided for information.

V ANALYTICAL ISSUES

NONE.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

259 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(18)47

The report of the EAG BIO meeting (17:11:17) was approved.

260 **Working Party BIO-DPS: Alternative Approaches for Documentary and Physical Standards for Biotechnological Products** COM(18)48

The report of the WP BIO-DPS meeting (17:05:18) was approved. This had been the first meeting of the Working Party and there had been a lot of discussion about basic concepts and the need for clarity. The members represented a diverse field from across the globe and had been very engaged. A teleconference had been held in October and the second meeting of the group would take place at the end of November.

261 **Expert Advisory Group MC1: Medicinal Chemicals** COM(18)49

The report of the EAG MC1 meeting (15:06:18) was approved and the following points were raised.

Ritonavir Preparations The EAG would be seeking advice from the Expert Advisory Group on Nomenclature regarding the chemical names of the impurities.

Paracetamol Preparations A wide-ranging review of the 17 Paracetamol-containing formulation monographs, including those for combination products, had been undertaken. It had been agreed to focus on the revision of the combination product monographs in the first instance, followed by the paracetamol only products.

262 **Expert Advisory Group MC2: Medicinal Chemicals** COM(18)50

The report of the EAG MC2 meeting (24:04:18) was approved.

263 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(18)51

The report of the EAG HCM meeting (22:06:18) was approved. The report highlighted the critical importance of DNA testing in the analysis of herbal materials.

264 **Panel DNA: Identification Techniques** COM(18)52

The report of the Panel DNA meeting (20:07:18) was approved and the following points were raised.

Cyperus rotundus The ITS2 reference sequence for *Cyperus rotundus* rhizome was ready to be published.

Outreach activities Dr Howard had given a keynote lecture at the United States Pharmacopeia during the summer, which illustrated that the work of the BP in this field was acknowledged internationally.

265 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(18)53

The report of the EAG BIO meeting (07:09:18) was approved and the following points were raised.

Interferon Alfa-2b Injection The EAG had discussed a number of options to address the exceptionally wide potency limits (75% to 135%), which included tightening the limits, removing the potency requirements and the Assay or omitting the monograph from a future edition of the British Pharmacopoeia.

Commission endorsed the recommendation to omit the monograph from the next edition of the BP.

Interferon Beta-1a Injection Different Assay and impurity limits were registered for different strengths of the product. In order to avoid widening the limits for the higher strength products EAG BIO had agreed that, exceptionally, these different limits should be specified in the monograph. Although unusual there was already precedence for this approach in a number of monographs and Commission endorsed the EAG's recommendation to include separate limits for the different strength products.

266 **Expert Advisory Group PCY: Pharmacy** COM(18)54

The report of the EAG PCY meeting (18:09:18) was approved. The majority of the meeting had been taken up with discussions about the BP dissolution policy, including the updates to the Appendix and Supplementary Chapter, and the proposals from the EDQM relating to the status of dissolution tests in finished product monographs. The consensus had been that dissolution tests should be included in finished product monographs, where possible, and that they should be mandatory.

VII EUROPEAN PHARMACOPOEIA

267 **European Pharmacopoeia Update** COM(18)55

European Pharmacopoeia Commission The draft report of the 161st Session of the EP Commission (June 2018) was available on the forum section of the BP website. The 162nd Session would be held between 19th and 20th November.

Members discussed items from the 161st session and items for the forthcoming November session and advised the UK delegation accordingly.

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.

Paediatric Formulary The first monographs developed by the Paediatric Formulary Working Party were now available for comment via the EDQM website.

VIII INTERNATIONAL COLLABORATION

268 **International Update** COM(18)56

Members were provided with an update on international activities.

United States Pharmacopeia A teleconference had been held in September to discuss: future monograph collaborations; the future of biological standards for the BP and the USP; progress on the Memorandum of Understanding between the two organisations; future issues for consideration at the International Meetings of World Pharmacopoeias.

USP Workshop on Analytical Procedure Lifecycle (Rockville, September) Dr Kemp had attended the workshop and had given a presentation on the BP project looking at how the principles of Quality by Design could be used by pharmacopoeias.

USP-FDA Workshop on DNA Standards for Botanical Identification Dr Howard had given the keynote lecture and taken part in a Panel Q&A session at the USP hosted workshop which had attracted attendees from industry, academia, trade associations and US government departments.

WHO Mr Evans had attended the 67th International Non-proprietary Names Consultation in October, during which proposals for 143 new chemical and biological names had been discussed. Mr Evans had been elected as Vice-Chair (Chemicals) for the meeting.

Compendial Joint Industry Meeting Mr Pound, Dr Lenihan and Dr Kemp had participated in this meeting with US industry groups by teleconference. The attendees had welcomed the early availability of the new BPCRS for the 2019 publications and the close engagement of the BP with stakeholders.

Laboratory Ms Li-Ship had attended a course in Strasbourg on the 2017 update to ISO 17025. This would help ensure that the BP Laboratory quality management system remained compliant with the current standard.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

269 European Pharmacopoeia Break-out Session

Mr Pound provided some additional information on the EDQM break-out session held to discuss the proposed adaptation of finished product monographs. Discussions would be continued at the November Session of the European Pharmacopoeia Commission.

X ANY OTHER BUSINESS

270 Cannabis

Following the introduction of legislation on 1st November 2018 regarding the rescheduling of Cannabis based products for medicinal use, the UK had been asked, exceptionally, to develop a monograph rapidly (the exact nature of the material covered by the monograph to be confirmed) in order to support national legislation.

This was an unusual situation and Commission would be kept informed of developments.

271 Items for Future Meetings COM(18)39

An updated list of items for discussion at future meetings was provided for information.

272 Date of next meeting

Tuesday 12th March 2019.