**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 11th November 2019.

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

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

Apologies for absence were received from Professor M Almond, Dr A M Brady and Dr P Varley.

Also present: Ms H Bowden, Ms H Corns, Mr P Crowley, Mr A Evans, Mr A Gibb, Mr G Kemp, Mr R Smith, Mr M Whaley and Mr S Young.

326 **Introductory Remarks**

**Welcome** The Chair welcomed members to the meeting. He also welcomed Ms Hannah Bowden and Mr Ryan Smith who had recently joined the Secretariat.

**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.

**MHRA** Dr Ian Hudson, former Chief Executive Officer of the MHRA, had retired in September. Dr June Raine, the former Director of the Vigilance and Risk Management of Medicines Division, had been appointed as the interim CEO until a permanent replacement was appointed.

**Members** This was the last meeting for Dr Lee, who would be retiring from Commission at the end of December 2019. It would also have been the last meeting for Professor Almond.

**Staff** Mr Himal Makwana had left the Secretariat at the end of July on transfer to the Defective Medicines Reporting Centre (Inspection, Enforcement and Standards Division). Ms Naomi Clothier had completed her fast-stream posting at the end of September.

**I MINUTES**

327 The minutes of the meeting held on 1st July 2019 were confirmed.

**II MATTERS ARISING FROM THE MINUTES**

328 The following matters arising from the meeting held on 1st July 2019 were noted.

**Minute 305 – BPCRS Establishment Policy** The changes to the BPCRS testing requirements had been agreed with the Laboratory. A note highlighting the changes had been sent to members and to the Chairs and Vice-Chairs of the Expert Advisory Groups.

**Minute 311 – Assay for Capsules; Minute 312 – Weight per mL Determinations in Assays for Liquid Preparations; Minute 313 – Correction factors: Use in Related substances tests** The outcomes from the discussions at the last meeting had been reflected in the updated Policy List.

## III REPORTS AND CORRESPONDENCE

### *GOVERNANCE*

329 **Operational Transformation**

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

330 **Lay Members Forum; Role of a Lay Member** COM(19)36

The Lay Members Forum (LMF) had been established in 2009 and comprised lay members from the BP Commission, the Commission on Human Medicines and the Expert Advisory Groups of CHM and the MHRA. The purpose of the LMF was to provide the members with a forum for peer support and the exchange of information.

An informal cross-agency group had been set up in 2018 to develop a generic role and responsibilities document for lay members participating in Advisory Committees (both Statutory and non-Statutory). A draft document had been prepared for discussion at the next meeting of the Lay Members Forum and was provided for information.

### *OPERATIONAL*

331 **Innovation Board Update** COM(19)37

**Overview of Delivered Improvements** Several key improvements to the BP website had been made in the last 12 months and website usage had been analysed.

***BPCRS*** CAS numbers had been included for a large number of BPCRS and a process for retaining previous leaflets had been established.

***BP User Guide*** The Guide had been issued in April and had been well received.

***Timeline feature*** Enhancements to the timeline feature had been introduced in August.

**User Research** Further research had been undertaken over the summer focusing on the theme of change in the pharmacopoeia.

**Tracked Changes** The first phase of the project to introduce tracked changes was on target for completion in late December. This would allow users to view additions/changes/deletions as either symbols and/or with the changes highlighted.

The second phase of the project was directed at including annotations to explain the rationale behind technical changes. This had been identified as a key feature for users during the research and it would reduce the regulatory burden associated with the annual publication cycle. The Secretariat was working with the publisher to develop a suitable way to display the information.

332 **AQbD Project Update** COM(19)38

**Consultation** A public consultation had been published on the GOV.UK website in June. The consultation had been widely publicised and presentations had been given at several events including the annual meeting of the Official Medicines Control Laboratories network, the Parenteral Drug Association Pharmacopoeia conference, a recent meeting of the Joint Pharmaceutical Analysis Group and during MHRA visits in China and the USA.

A formal response to the consultation would be prepared by the cross-agency working group and would be published on the GOV.UK website in the new year.

**AQbD Working Party** A workshop had been held to consider how best to proceed with the project.

333 **MHRA Strategy for Pharmacopoeial Quality Standards for Biological Medicines: Update** COM(19)39

Mr Gibb provided an update on activities associated with the MHRA Strategy relating to the development of documentary and physical standards for Biological Medicines.

334 **BPCRS Establishment Policy: Results of Laboratory Trial** COM(19)40

**Results of Trial** A trial had been undertaken consisting of live data generated by the injection of disregard solutions at both 0.05% (BP) and at 0.03% (Ph Eur) and a paper review of previously completed BPCRS re-test results.

**Assessment** The results had indicated that a change to adopt the Ph Eur approach should be feasible. It would also offer the advantages of providing a more accurate declared content figure and a harmonised approach.

**Proposal** Based on the results of the trial, and with a view to harmonisation and increased accuracy, the Laboratory had proposed that the BPCRS declared content policy should be amended to adopt a disregard limit of 0.03% as the default value.

It was agreed that the change should not be applied retrospectively but should only be applied to new, replacement and re-test BPCRS.

335 **British Pharmacopoeia Laboratory** COM(19)41

**British Pharmacopoeia Laboratory Reports** The list of 25 reports concerning new and revised monographs that had been prepared by the Laboratory since the July 2019 meeting was provided for information.

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

## IV FUTURE PUBLICATIONS

336 **Monograph Portfolio Review** COM(19)42

**Phase 1** The first stage of the monograph portfolio review had identified about 200 monographs which had been reviewed taking into consideration factors such as: whether products were licenced in the UK; the number of Marketing Authorisation Holders; usage

figures; the critical need of particular products for patients; if the product was included on the WHO List of Essential Medicines.

Proposals had been presented at recent EAG meetings, resulting in a list of 24 monographs proposed for omission from the BP 2021 publications, subject to confirmation from EAGs which had yet to meet. The list of monographs would be circulated to international contacts and the Expert Advisory Group on Unlicensed Medicines to ascertain if any of the items were still used overseas or were available as unlicensed formulations. The finalised list of monographs for omission from the BP 2021 and BP (Vet) 2021 would be presented at the April 2020 meeting.

**Phase 2** The second stage of the review would be directed at monographs containing out-dated technology. The Secretariat would be working closely with the publisher to identify affected monographs and these would be reviewed in line with the Guiding Principles, which were now finalised.

337 **Approved Synonyms** COM(19)43

**New monographs** The proposed new Approved Synonyms relating to items added to the European Pharmacopoeia by means of the 10th Edition were approved. The items would be added to Appendices XXI B and XXI B (Vet) by means of the BP 2021 and would be incorporated within the online updates to the BP 2020 publications. For the remaining new monographs included in the 10th Edition, members recommended that the Ph Eur titles should be used.

**Title changes** The title of the monograph for ***Yersiniosis Vaccine (Inactivated) for Salmonids*** had been changed to ***Enteric Redmouth Disease Vaccine (Inactivated) for Rainbow Trout***. Advice had been received that the current approved synonym for this material should be retained and the Appendix entries would be amended to reflect the new Ph Eur title.

## V ANALYTICAL ISSUES

338 **Expression of Related substances Limits** COM(19)44

**Background** The method of expressing the limits in Related substances tests had last been discussed in 2015. It had been agreed that the impact of moving from the current approach, which included limits based on the comparison of peak areas, to the numerical limits approach adopted by the European Pharmacopoeia should be examined.

**Impact on Users** ***Benefits*** It was noted that a change to the inclusion of numerical limits provided the opportunity to present the acceptance criteria in a clearer format that was aligned with modern laboratory practices and should remove some of the issues that users had reported in interpreting and calculating impurity limits.

**Impact on Secretariat and Laboratory** ***Benefits*** The change to numerical limits would demonstrate that the BP had responded to user feedback regarding the need for clarity in monographs and the inclusion of methods and practices that were aligned with those used in their organisations. The Laboratory already reported impurities in terms of numerical limits and so there would be no need to change the way results were presented.

***Risks*** It was noted that additional technical considerations would need to be taken into account as the way the limit was expressed affected how it was interpreted. The Secretariat would need to ensure that a consistent approach was adopted across the EAGs.

***Resources*** There would be significant resource implications if all affected monographs were to be updated in a single edition of the BP. However, this could be managed if the approach was restricted to new monographs and those undergoing technical revision.

**Discussion** Members supported the move towards the inclusion of numerical limits in BP monographs for both active substance and product monographs, in line with the Ph Eur. An example of how a future BP Related substance test might appear had been provided and was agreed.

**Next steps** The Secretariat would carry out a stakeholder consultation in the first part of 2020 regarding the proposed introduction of numerical limits into BP monographs.

339 **New Analytical Technologies** COM(19)45

**Background** The *ad-hoc* group on New Analytical Technologies had been established in 2017 with the remit of: (1) exploring ways of identifying new analytical technologies; (2) designing a decision-making process in order to take appropriate action forward; (3) making recommendations on the management and approval of decisions. Since the last update to Commission, workshops had been held with members of the *ad-hoc* group, the BP and Laboratory Services team and Agency colleagues.

**Evaluation and approval** An evaluation and approval process had been developed by the *ad-hoc* group together with a guidance document intended to support the Secretariat in the evaluation of new analytical technologies.

***Liquid Chromatography/UV Diode Array Detection (LC/UV-DAD) for Identification*** Proposals to introduce identification tests using LC/UV-DAD had been prepared and agreed by the *ad-hoc* group. The intention was to include such tests in BP monographs, where appropriate, subject to the outcome of a public consultation.

***Pulsed Electrochemical Detection with Liquid Chromatography*** Proposals to include HPLC methods using pulsed electrochemical detection (PED) were in development and would be brought to members' attention at a future meeting.

340 **Aide Memoire** COM(19)46

The Aide Memoire had been developed as a guidance document intended to assist in the development and revision of BP monographs and was for use by the Secretariat, the BP Commission and the Expert Advisory Groups.

The document had been updated to reflect changes since the last version had been issued in 2017, together with several additional changes for clarity.

341 **Policy List** COM(19)47

The Policy List had been prepared as a reference source of key policies relating to BP monographs to assist Commission members in their BPC/EAG work and when reviewing text for the annual BP publications.

The Policy List had been updated to reflect changes since the first version had been issued in 2017, together with several additional changes for clarity.

## VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

342 **Expert Advisory Group ABS: Antibiotics** COM(19)48

The report of the EAG ABS meeting (07:02:19) was approved and the following point was raised.

**Phenoxymethylpenicillin Preparations** During revision of the formulation monographs the EAG had noted that as 4-hydroxyphenoxymethylpenicillin ("impurity D") was listed as an active moiety it should not be referred to as an impurity. It had been agreed that a request for revision should be submitted to the European Pharmacopoeia Commission to correct the monographs for Phenoxymethylpenicillin and Phenoxymethylpenicillin Potassium accordingly.

343 **Expert Advisory Group MC2: Medicinal Chemicals** COM(19)49

The report of the EAG MC2 meeting (13:06:19) was approved and the following points were raised.

**Control of nitrosamines** Further to the issues with the -sartans, nitrosamine impurities had now been detected in ranitidine products. A number of ranitidine-containing products had been recalled in the UK and EU Member States and testing was being carried out by the Official Medicines Control Laboratories.

**Carbocisteine Preparations** Development of the new formulation monographs was in progress, subject to further revision of the Ph Eur monograph for Carbocisteine.

**Methylphenidate Prolonged-release Preparations** The Laboratory had been unable to develop an extraction procedure that was suitable for application to all available formulations. Members had discussed potential ways to resolve the issue, which might affect other prolonged-release products. Further Laboratory work would be carried out before any proposals could be made.

344 **Expert Advisory Group MC1: Medicinal Chemicals** COM(19)50

The report of the EAG MC1 meeting (25:06:19) was approved.

345 **Working Party BIO-DPS: Alternative Approaches for Documentary and Physical Standards for Biotechnological Products** COM(18)51

The report of the WP BIO-DPS meeting (08:08:19) was approved.

346 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(19)52

The report of the EAG BIO meeting (13:09:19) was approved and the following points were raised.

**Heparin Injection** Work was being undertaken at NIBSC to support revision of the monograph for Heparin Injection, including the use of nuclear magnetic resonance spectrometry as a means of identification.

## VII EUROPEAN PHARMACOPOEIA

347 **European Pharmacopoeia Update** COM(19)53

**European Pharmacopoeia Commission** Members discussed items from the 164th Session of the EP Commission (June 2019) and advised the UK delegation accordingly.

**Dissolution Testing** A joint EDQM/BP webinar had been held on 15th October. Over 80 participants had joined the webinar and positive feedback had been received.

**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

348 **International Update** COM(19)54

Members were provided with an update on international activities.

**MHRA Visit to the USA** Mr Pound and Mr Gibb had visited the USA in July and had attended several meetings with key regulatory and industry stakeholders.

***USP*** A bilateral meeting had been held at the USP headquarters during which a range of topics had been discussed, including: future strategy and direction. A Memorandum of Understanding between the BP/MHRA and USP was signed during the meeting which would serve as a foundation for greater collaboration and knowledge-sharing in the future.

***US Compendial Affairs Group*** A general update on high level BP projects had been provided, together with an update on current BP activities.

***Stakeholder meeting*** A meeting with key US standards setting stakeholders for ATMP had been held. This included representatives from US government initiatives such as the Standards Coordinating Body and the US FDA Office of Tissue and Advanced Therapies.

**European Medicines Agency Naming Review Group** Mr Evans had attended the most recent meeting in September, at which over 100 new names had been discussed. The names were intended for future Centralised licence applications and had to be acceptable in all Member States. The group had previously supported the BP/MHRA proposals for the naming of liposomal formulations and there was now a requirement for the term “liposomal” to be included in the name of products where the posology of the formulation permitted a higher amount of the product to be administered to patients than of the corresponding non-liposomal formulation.

**Future look** The 11th International Meeting of World Pharmacopoeias would be held in Strasbourg in February 2020 and would include a session for interested stakeholders. The 70th INN Consultations would be held in Geneva in April 2020.

## IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

### 349 MHRA

Dr Sarah Branch had been appointed as the interim Director of the Vigilance and Risk Management of Medicines Division. Mr John Wilkinson had retired from his post as Director of the Devices Division and Mr Graeme Tunbridge had been appointed as the interim Director of Devices.

### 350 Agency Board

A paper would be presented at a future meeting of the Agency Board on the role that standards (including those in the BP) can play in supporting innovation.

## X ANY OTHER BUSINESS

### 351 BP and MHRA

The Chair welcomed Dr Raine, interim CEO, to the meeting. Dr Raine thanked members on behalf of the MHRA for their selfless service and huge commitment to public health. She thanked Dr Lee for the contributions he had made during his time as Secretary and Scientific Director and as a member of the BP Commission and also Professor Almond.

### 352 Retiring Members

The Chair paid tribute to Dr Lee and thanked him for his long service, dedication and commitment to the work of the BP and the BP Commission over many years. Dr Lee had been Secretary and Scientific Director of the BPC between 2002 and 2011 and had been a member of the Commission since 2012. He had been instrumental in establishing the Expert Advisory Group on Unlicensed Medicines and had been actively involved with the work of EAG ULM throughout his association with the BP Commission. He would continue to serve as Chair of EAG ULM. Dr Lee had also been actively involved in the work of the European Pharmacopoeia Commission, formerly serving as Chair of the Expert Group on Medicinal Gases and the Working Party on Water for Pharmaceutical Use and as a member of the Working Party on Pharmaceutical Preparations. The Chair said he would miss Dr Lee's humour and wisdom and wished him well in his retirement. Dr Lee thanked the Chair for his kind words and said that although he would be sorry to leave, he felt it was an appropriate time to say goodbye.

The Chair also paid tribute to Professor Almond who had joined the Commission in 2016. Professor Almond would remain as Chair of Expert Advisory Group MC3: Medicinal Chemicals and as a member of the Panel of Experts on Inorganic and General Chemicals but would stand down from the *ad-hoc* group on New Analytical Technologies.

### 353 Date of next meeting

Monday 6th April 2020.

**FOR INFORMATION:**

354 **British Pharmacopoeia 2021: Text Review Dates**

The dates for reviewing the BP 2021 and BP (Vet) 2021 text using the document review tool (DRT) were provided for information.

355 **Items for Future Meetings**

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