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 1st July 2019.

Present: Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), 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 Professor M Simmonds.

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

Apologies for absence were received from Professor M Almond, Dr R Torano and Dr P Varley.

Also present: Ms H Ashraf, Ms N Clothier, Ms H Corns, Mr P Crowley, Mr A Gibb, Mr G Kemp, Ms G Li-Ship, Mr H Makwana, Mr M Whaley and Mr S Young.

298 **Introductory Remarks**

Welcome The Chair welcomed members to the meeting. He also welcomed Ms Graziella Li-Ship, BP and Laboratory Services.

Staff Ms Sarah Gomersal had recently left the Secretariat and had transferred to the Inspectorate (Pharmacovigilance Group). Mr Laxsaan Elanganathan had re-joined the Secretariat in April, after spending 9 months in the Inspection Action Group of the Inspection, Enforcement and Standards Division.

Obituary Members were saddened to learn of the death of Professor Peter Hylands, former Head of the Pharmacy Department at Kings College, London. Professor Hylands had been a member of the Expert Advisory Group on Herbal and Complementary Medicines until 31st December 2014.

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

299 The minutes of the meeting held on 12th March 2019 were confirmed.

II MATTERS ARISING FROM THE MINUTES

300 The following matters arising from the meeting held on 12th March 2019 were noted.

Minute 285 – Monograph Initiation: Candidate Monographs The new formulation monographs had been added to the BP Work Programme as agreed. The Secretariat would liaise with the EDQM regarding the potential addition of new drug substance monographs to the European Pharmacopoeia Work Programme at a suitable opportunity.

Minute 296 – Expert Advisory Groups, Panels of Experts and Working Parties
Dr Gillian Clarke had accepted the invitation to join the Expert Advisory Group on Antibiotics. Dr Phil Borman had accepted the invitation to join the Working Party on Analytical Quality by Design.

III REPORTS AND CORRESPONDENCE

GOVERNANCE

301 Operational Transformation

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

302 Future Laboratory Provision COM(19)18

Background and current contract The current BP/MHRA Laboratory service was provided by the Laboratory of the Government Chemist (LGC) in Teddington. This included work to support public health incidents, together with developing analytical methods and establishing and maintaining BPCRS to support BP monographs. The current contract would expire in March 2021.

Invitations to submit bid applications for the new contract would be issued during the 2019-2020 financial year, with the aim of awarding a contract about 12 months before the current contract expired. Commission would be kept informed of developments.

OPERATIONAL

303 Innovation Board Update COM(19)19

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

Ongoing research A programme of ongoing research had recently been approved by the Innovation Board. This was intended to ensure that the research was kept up-to-date, to monitor the implementation and success of changes over time and to identify additional areas for improvement.

Innovation Board Outputs Positive feedback had been received in response to the BP User Guide which had been downloaded over 800 times since its launch. The key projects for the immediate future were (i) to develop a suitable way to identify amendments in the BP by the use of tracked changes and (ii) to modify the current timeline feature to highlight editions of the BP in which a particular monograph had been amended (scheduled for release with the BP 2020).

304 AQbD Project Update COM(19)20

A public consultation on the application of Analytical Quality by Design (AQbD) principles to pharmacopoeial standards had been published in June on the GOV.UK website and would be open until the end of August. It included examples illustrating how the adoption of AQbD principles might appear in monographs, together with a technical document outlining the work undertaken to date.

305 **BPCRS Establishment Policy** COM(19)21

The current BPCRS catalogue contained over 800 items required to support BP monographs. The Laboratory carried out a series of tests during the establishment, replacement and re-testing of BPCRS to ensure the suitability of the materials for their intended use.

General BPCRS Establishment Policy The tests carried out during the establishment of a BPCRS generally included: Appearance/ Description; Identification; Related substances / Chromatographic Purity; Water / Moisture; Assay. The Secretariat and Laboratory had reviewed the current approaches and had proposed a number of changes which were intended to ensure the most efficient use of Laboratory time and resources while maintaining the same level of quality.

The Secretariat would inform the Laboratory of the Commission's discussions and the revised proposals would be incorporated within the Laboratory policy documents. The changes would affect the information included in the BPCRS reports that were provided to the Chairs and Vice-Chairs of the analytical Expert Advisory Groups for approval. Guidance would be provided to the Chairs and Vice-Chairs and the wider Commission before the changes were implemented.

Assignment of Purity Value Policy Declared content figures were calculated from the results of a chromatographic purity test and a test for Water. The current policy when assessing the results was to include the total amount of impurities above the monograph disregard limit and to exclude impurities below this limit. It was stated that this approach might not always be suitable, i.e. where there were several impurities just below the disregard limit which could lead to a significant number of peaks not being included in the total impurity limit, thereby potentially leading to the assignment of an incorrect declared content value.

The Laboratory had proposed carrying out a trial to ascertain if adopting the Ph Eur approach regarding the disregard limits would make a significant impact on the results. Members agreed that the BP policy should be harmonised with that of the EP, if feasible, and endorsed the proposal for a Laboratory trial.

306 **British Pharmacopoeia Laboratory** COM(19)22

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

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

IV FUTURE PUBLICATIONS

307 **BP 2020; BP (Vet) 2020**

The Chair thanked members for their review of the second batch of text for the BP 2020 and BP (Vet) 2020 and he praised the Secretariat for the quality of the draft text.

308 **BP Work Programme** COM(19)23

A high-level summary of the BP work programme relating to new and revised monographs across the Expert Advisory Groups was provided. This included indicative numbers of texts for inclusion in the next three editions of the British Pharmacopoeia.

309 **Monograph Portfolio Review** COM(19)24

At the last meeting members had been informed of the intention to carry out a full and systematic review of the current monograph portfolio and BPCRS catalogue in order to ensure that resources were directed towards maintaining and improving those monographs that were considered to be of most value to users. A set of draft principles had been presented which provided criteria which could be used to decide whether a current monograph should be retained, amended or omitted. Further work had been undertaken to identify an efficient means of carrying out the review in a realistic time-frame.

Phase I During phase I of the review it was intended to identify and remove or amend monographs that were no longer perceived to add value to users.

Phase II After the first phase of the review was completed, the intention was to focus on monographs that contained outdated methodology with a view to improving the quality of current standards. Commission would be kept informed of developments.

310 **Monographs for Omission from the BP 2020: Update** COM(19)25

The monographs proposed for omission from the BP 2020 publications had been posted on the BP website in March and had been provided to several international contacts in countries where the BP was used. Requests to retain a number of monographs had been received. The Secretariat responsible for the specific monographs had reviewed the specific items before deciding whether they should still be omitted or if they should be retained for the shorter or longer term, taking into consideration factors such as the continued use of the products outside the UK, items no longer recommended for use and the feasibility of updating outdated methods. This had resulted in the retention of 20 monographs in the BP 2020 that had previously been agreed for omission.

V ANALYTICAL ISSUES

311 **Assay for Capsules** COM(19)26

An inconsistent approach in the method of sample preparation in the Assay for tablets and capsules had been highlighted. Whereas the approach for tablets was to “Weigh and powder 20 tablets”, the usual approach for capsules specified using “the mixed contents of 20 capsules” without an explicit weighing step.

The Secretariat had proposed a form of words that would encompass powder-, granule- and liquid-filled capsules, which was accepted. It was agreed that the wording should be included in all new capsule monographs from the BP 2021 onwards, although it was recognised that there may be cases where it was not appropriate, for example in those methods that specified the use of whole capsules. It was agreed that existing monographs should be updated during routine revisions.

312 **Weight per mL Determinations in Assays for Liquid Preparations** COM(19)27

The current policy was that weight per mL requirements were only included in monographs for oral liquid formulations. It had been recommended that the current policy should be reviewed and the Secretariat had proposed a number of options for consideration.

The Secretariat had not received any indications that the current approach was causing issues for users. It was agreed that there was a need for a clear policy to be in place, but that a pragmatic approach should be adopted for new and revised monographs rather than imposing rigid requirements. It was agreed that in general: for non-viscous liquids, sampling by volume would be specified; for viscous liquids, sampling by weight would be specified and a weight per mL requirement included in the Assay.

313 **Correction factors: Use in Related substances tests** COM(19)28

The current approach to the use of correction factors was outlined in Supplementary Chapter I A: Control of Impurities and in Appendix III: Chromatographic Separation Techniques.

Attention had been drawn to the policy included in the European Pharmacopoeia Technical Guide which stated that "*Usually, no correction factor will be given if the reported batch values for an impurity are below the applicable limit for unspecified impurities before correction and below the reporting threshold (disregard limit) after correction*". In practice the Ph Eur approach was to include a correction factor for specified and unspecified impurities if a pass or fail decision was affected by application of the correction factor.

While members were generally supportive of adopting the Ph Eur approach for new BP monographs, it was agreed that a pragmatic approach should be adopted and that retrospective changes were not required.

VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

314 **Working Party BIO-DPS: Alternative Approaches for Documentary and Physical Standards for Biotechnological Products** COM(18)29

The report of the WP BIO-DPS meeting (28:11:18) was approved. The meeting had focussed on the different proposed approaches to monograph development (performance-based, method capability-based, structural-class based, etc.) and it had been recognised that a combination of approaches might be required. The group had also discussed how Analytical Quality by Design principles could be used in the development of biological/biotechnological monographs. Initial work would be carried out on monoclonal antibodies and practical work had been started on a donated product.

315 **Expert Advisory Group NOM: Nomenclature** COM(19)30

The report of the EAG NOM meeting (12:02:19) was approved and the following points were raised.

British Approved Names 2017: Supplement No. 3 The Supplement had been sent to TSO and would be published at the same time as the BP 2020 publications.

Liposomal Formulated Medicines The EMA Naming Review Group had supported the BP/MHRA proposals for the naming of liposomal formulations using the modified BAN/INN approach as the safest way to name these medicines.

MHRA Guidelines for the Naming of Medicinal Products and Braille Requirements for Name on Label The updated guidance had recently been issued and was available on https://www.gov.uk/government/publications/naming-human-medicines.

316 **Panel DNA: Identification Techniques** COM(19)31

The report of the Panel DNA meeting (12:02:19) was approved. This had been the last meeting of the Panel, which had been now been disbanded. The exceptional work undertaken by the Herbals team had been acknowledged and tribute had been paid to current and former members of the Panel for their invaluable contributions and support over the last few years.

317 **Expert Advisory Group MC3: Medicinal Chemicals** COM(19)32

The report of the EAG MC3 meeting (26:02:19) was approved.

VII EUROPEAN PHARMACOPOEIA

318 **European Pharmacopoeia Update** COM(19)33

European Pharmacopoeia Commission The draft report of the 163rd Session of the EP Commission (March 2019) was available on the forum section of the BP website. The 164th Session had been held on 18th June.

Members discussed items from the 163rd and 164th Sessions and advised the UK delegation accordingly.

10th Edition of the European Pharmacopoeia An international conference had been held by the EDQM (19th to 20th June) to celebrate the publication of the 10th Edition of the European Pharmacopoeia and the 25th anniversary of the establishment of the OMCL network and the Certification procedure. This had been attended by Mr Makwana and members of the UK delegation. The conference had comprised two plenary sessions and workshops on Impurities, Biotherapeutics, General Methods, Finished Product Monographs, Certification, Advanced Therapy Medicinal Products and the OMCL Network.

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

319 **International Update** COM(19)34

Members were provided with an update on international activities.

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.

INN Consultations Mr Evans had attended the 68th International Non-proprietary Names Consultations, held in Geneva, and had been elected as Vice-Chair for discussions on chemical entities.

WHO Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeial Specifications for Medicines Ms Corns had attended the consultation, during which the first BP/International Pharmacopoeia informally harmonised monograph for Moxifloxacin Tablets had been finalised.

European Medicines Agency Naming Review Group Mr Evans had attended this meeting, which was the first to be held in the interim building in Amsterdam following the departure of the EMA from London. The names were intended for future Centralised licence applications and had to be acceptable in all Member States.

Parenteral Drug Association (PDA) Pharmacopoeias Conference Mr Pound and Mr Gibb had attended the 2nd PDA Conference on International Developments in the Pharmacopoeial Landscape, held in Geneva. The main focus of the event was a workshop split into streams on Analytics, Biotherapeutics and Continuous Manufacture. Mr Pound had given a presentation on Analytical Quality by Design and the Pharmacopoeia, which had been well received. Dr Cook had also attended the event and had presented on AQbD and on continuous manufacture.

PDA Advanced Therapy Medicinal Products Conference Mr Gibb had attended this event, held in Vilnius, which had brought together experts and speakers on cell and gene therapies. Positive feedback had been received regarding the BP/MHRA approach for the regulation of these products.

China Mr Pound had recently attended several meetings in China: CPhI, Shanghai, which had included a session on updates from international regulators; the Symposium on International Standards Formulation and Certification; the Symposium on the History of World Wide Pharmacopoeias, which had included the opening of the Museum of Pharmacopoeias.

320 **OMCL Annual Meeting – London 2019** COM(19)35

The 24th Annual Meeting of the Official Medicines Control Laboratories (OMCL) Network had been co-hosted by the MHRA, NIBSC and the Veterinary Medicines Directorate (VMD) in May. The network comprised over 70 different laboratories from 40 countries. The event had been a great success, with 260 delegates attending various sessions which had been chaired by MHRA, NIBSC or VMD staff, as appropriate, with EDQM staff as Co-Chair.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

321 **MHRA**

The current Chief Executive of the MHRA, Dr Ian Hudson, would be standing down at the end of September and a new CEO should be in place at the time of the next meeting.

X ANY OTHER BUSINESS

322 BPC Appointments

The Secretariat was working with the Appointments Team at the Department of Health and Social Care regarding future appointments and re-appointments to the BP Commission.

323 Meeting Minutes

Members were reminded that the full minutes for BPC and EAG meetings were provided as a comprehensive formal record of the meeting discussions. Summary minutes were provided in response to the introduction of the Freedom of Information Act 2000 and the statutory requirement to provide public access to information.

324 Date of next meeting

Monday 11th November 2019.

FOR INFORMATION:

325 Items for Future Meetings

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