

**SUMMARY MINUTES**  
**of the**  
**BRITISH PHARMACOPOEIA COMMISSION**

A meeting of the British Pharmacopoeia Commission was held at 151, Buckingham Palace Road, London SW1W 9SZ on Monday 22<sup>nd</sup> September 2014.

**Present:** Professor K Taylor (*Chair*), Professor A G Davidson (*Vice-Chair*), Mr B J Capon (*Lay Member*), Professor D Cairns, Dr G Cook, Mr A Coulson, Mr C T Goddard, Dr K Helliwell, Dr R L Horder, Dr M G Lee, Professor J Miller, Dr R Torano, Dr L Tsang, Mrs J M Turnbull, Professor E Williamson.

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

Apologies for absence were received from Dr B Matthews and Dr P Varley.

Also present: Mrs M Barrett, Ms H Corns, Mr A Evans, Mr A Gibb, Dr P Holland, Dr C Howard, Dr R A Pask-Hughes, Miss C Pitt, Mr J Pound, Mrs M Vallender, Mr M Whaley and Mr S Young.

875 **Introductory Remarks**

**British Pharmacopoeia 2015** The BP 2015 and BP (Vet) 2015 had been published on 26<sup>th</sup> August and would come into effect on 1<sup>st</sup> January 2015.

**Congratulations** Members were pleased to note the marriage of Mr Peter Crowley, which had taken place on 21<sup>st</sup> September.

**Annual Report** A letter had been received from Earl Howe (Parliamentary Under Secretary of State for Quality) on behalf of the UK Health Ministers thanking the Chair for the 2013 BP Annual Report and recognising the contribution from members throughout the year.

**Declaration of Interests** 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.

**I MINUTES**

876 The minutes of the meeting held on 17<sup>th</sup> March 2014 were confirmed.

**II MATTERS ARISING FROM THE MINUTES**

877 The following matters arising from the meeting held on 17<sup>th</sup> March 2014 were noted.

**Minute 847 – Appraisals** Appraisals for all members had been completed and forwarded to the Department of Health.

**Minute 856 – BP 2015: Text for approval** The Chair thanked members for their comments on the BP 2015 text and noted that, for future publications, the Secretariat would be looking into ways of providing feedback on the comments raised.

**Minute 857 – Monographs for Omission from the BP 2015 and BP (Vet) 2015** Amphotericin Lozenges and Amphotericin Oral Suspension were no longer licensed in the UK and these monographs had also been omitted from the BP 2015.

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**Minute 858 – Approved Synonyms** In view of changes to a number of Ph Eur monograph titles in Supplement 8.2, a number of additional approved synonyms and title changes relating to monographs for Materials used in the Manufacture of Homoeopathic Preparations had been included prior to finalisation of the BP 2015.

**Minute 859 – British Approved Names 2012: Supplement No. 3** The draft Supplement had been sent to members during May for comment. The amended text had been published in August and would come into effect on 1<sup>st</sup> January 2015.

**Minute 862 – Analytical Quality by Design Working Party** All the candidate members had accepted the invitation to join the new Working Party.

### III REPORTS AND CORRESPONDENCE

#### 878 Chloroform-containing Preparations COM(14)22

At the December 2013 meeting it had been agreed that, in view of the ongoing discussions within the MHRA and the recommendations of the Commission on Human Medicines, all references to the use of chloroform as a pharmaceutical ingredient should be removed from the British Pharmacopoeia at the earliest opportunity (minute 826 refers).

The Commission's discussions had been drawn to the attention of the Expert Advisory Groups and Panels of Experts who had responsibility for the affected monographs. There had been overwhelming support for the removal of chloroform as an ingredient and members were invited to consider the following proposals:

- 1. For monographs including chloroform as part of an extemporaneous preparation:** The formula and/or method of preparation to be removed by means of the BP 2016.
- 2. For monographs including chloroform in the title:** The monographs to be omitted from the BP 2016.

Members endorsed the proposed recommendations.

#### 879 Unlicensed Medicines: Progress Report COM(14)23

Members were provided with a progress report relating to the work of the Expert Advisory Group on Unlicensed Medicines.

**Introduction** The suggestion to include monographs for unlicensed medicines in the BP had arisen following a discussion on monograph initiation policy during 2004-2005. It had been agreed that, in view of the continued and widespread use of unlicensed medicines in the UK, the provision of publicly available BP standards would be a valuable addition to the BP.

**Monographs and Other Texts** Since 2007, a total of 68 monographs for unlicensed formulations had been published, together with a General Notice, a General Monograph and six Supplementary Chapters on Unlicensed Medicines. The inclusion of the opening statement “[*Monograph Title*] *is/are not currently licensed in the United Kingdom*” facilitated the transfer of monographs to other EAGs in the event that a product received a license.

**Work Programme** A copy of the work programme for EAG ULM was provided for information.

**Development of Monographs** The monographs followed the format of those for licensed preparations and were mainly written as open format texts.

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**Future Issues** It was becoming increasingly difficult to obtain data to support the development of robust monographs for unlicensed medicines. EAG ULM were considering areas for which it might be possible to provide information in the form of Supplementary Chapters.

**Discussion** A member asked why there were so many widely used medicines that were unlicensed. In many cases it was due to the need for liquid formulations, for example in the case of paediatric medicines where the patient was unable to take tablets or capsules. UK Medicines legislation allowed the use of unlicensed medicines to meet the special needs of patients that could not be met by current licensed products.

Members were concerned at the problems with obtaining adequate data on widely used unlicensed medicines and it was suggested that methods could be developed by university students. It was noted that proposals for monographs had been received from a limited number of sources and that by contacting other NHS Units it might be possible to generate additional information. Information on the usage of unlicensed medicines was not as readily available as that for licensed products, but this would also be taken into account in any future prioritisation exercise.

### 880 **BP/NIBSC Biologicals Project** COM(14)24

A summary of the outcomes of a meeting between representatives from the BP Secretariat and NIBSC was provided for information and attention was drawn to the following points.

**BP Monograph Elaboration and Development of BP Biological Reference Preparations (BPBRP)** Desmopressin had been chosen for use in the pilot study to develop a BP secondary biological reference preparation. The material was widely used in the UK and there were three published monographs and two monographs on the work programme for Desmopressin formulations. It was anticipated that testing based on HPLC would be suitable.

While members generally supported the principle of developing secondary standards there were a number of issues for clarification, such as: whether the material should be described as a “reference standard” or a “reference preparation”, whether the secondary and primary standards could be used interchangeably and the pricing policy. It was agreed that EAG BIO should give further consideration to the feasibility of this project and to consider the points raised by members.

**Review of Available Reference Materials at NIBSC** In view of the availability of surplus materials, the possibility of developing secondary biological reference standards to support a number of BP monographs was being considered.

### 881 **Structure and Content of BP Monographs for Herbs used in Traditional Herbal Medicines** COM(14)25

**Structure and Content of Published BP and Ph Eur Monographs** BP herbal monographs typically consisted of microscopical, macroscopical and chromatographic identification tests, appropriate physical tests, tests for adulterants and an Assay. Where an Assay was included it was generally HPLC or the GC profile of the essential oil and a content statement providing limits for either a compound of known therapeutic activity or a marker compound was included under the Definition. It was noted that marker compounds did not affect the activity of the herb.

**HPTLC Identification** Thin-layer chromatography (TLC) had been traditionally used as an identification method for herbal materials. There was now a trend towards the use of high-performance TLC (HPTLC) which could also be used as a semi-quantitative method to obtain data on the levels of marker compounds. The BP Secretariat was carrying out a project to develop HPTLC methods for the identification of herbal drugs with a view to inclusion in future BP monographs.

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**Routine Inclusion of Assay Methods** The Expert Advisory Group on Herbal and Complementary Medicines had reviewed the policy on the inclusion of Assays in BP monographs for Herbs used in Traditional Herbal Medicines at their June meeting.

The need for the routine inclusion of an assay was being questioned in cases where the herb was used in a traditional sense, for example when used to prepare a decoction by the patient or herbal practitioner. It was recognised that the formulations might vary and that a number of herbs could be used interchangeably. In these instances it was more important to ensure that the herb could be correctly identified and its microbial quality assured rather than for the amount of a marker compound to be within defined limits. In addition there was the possibility that the amount of “active” compound could be reduced when it was extracted and used to prepare a herbal medicinal product.

Commission endorsed the proposal that the inclusion of assays in monographs for herbs used in Traditional Herbal Medicines should be considered on a case-by-case basis.

882 **British Pharmacopoeia Laboratory** COM(14)26

**British Pharmacopoeia Laboratory Reports** The list of reports concerning new and revised monographs that had been prepared by the Laboratory since the March 2014 meeting was provided for information.

**British Pharmacopoeia Chemical Reference Substances** The list of reports concerning British Pharmacopoeia Chemical Reference Substances (BPCRS) that had been tested since the March 2014 meeting was provided for information.

883 **BPCRS: User Guidance** COM(14)27

Further to the discussions at the March 2014 meeting (minute 855 refers), the Secretariat had sought legal advice regarding the action to take in the event that a BPCRS required to support a monograph was not available.

The lawyers had advised that, under the Human Medicines Regulations 2012, the BP could include provisions to allow the use of an alternative reference standard should the official material be unavailable for any reason.

It had been suggested that the General Notice on Assays and Tests should be expanded to permit the use of alternative reference standards in order to demonstrate compliance and a draft amendment had been prepared for consideration.

Several members were of the opinion that no change to the General Notice should be made and that it would be better to carry out a risk assessment to identify those BPCRS most at risk of falling out of stock and to take action as necessary. It was noted that problems would only arise if orders for out of stock material were received.

It was agreed that this matter should be given further consideration by the Secretariat before any action was taken.

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### IV FUTURE PUBLICATIONS

#### 884 **Monograph Initiation: Candidate Monographs** COM(14)28

A request had been received for the BP to elaborate a monograph for e-cigarettes. This was to support the UK position that e-cigarettes which were above a certain strength and total nicotine content and/or those with a medicinal claim should be required to hold marketing authorisations.

Members agreed that since these products were prescribed and were widely available a BP monograph should be elaborated. However, in view of the nature of the products the need to liaise closely with relevant parts of the MHRA, such as the Devices division, and other organisations was acknowledged. Commission would be kept informed of developments.

#### 885 **Approved Synonyms** COM(14)29

**New Monographs** The draft list containing a number of new Approved Synonyms relating to items added to the European Pharmacopoeia by means of Supplement 8.3 was approved. The items would be added to Appendix XXI B in the next edition of the BP. For the remaining monographs, members recommended that the Ph Eur titles should be used.

**Title Changes** Following a change in the title of the monograph for Human Normal Immunoglobulin, advice had been received that the title in the BP should reflect the new Ph Eur title and the entry in Appendix XXI B amended accordingly. Members endorsed this change. The definition for Alendronic Acid Tablets would be amended to reflect the change in the title of the Ph Eur monograph for Sodium Alendronate.

**British Approved Names** As a consequence of an addition to the Ph Eur, Meldonium (anti-ischemic drug) would be added as a new British Approved Name in a future BAN publication.

### V ANALYTICAL ISSUES

#### 886 **Aide Memoire** COM(14)30

The Aide Memoire had been updated in accordance with the changes agreed at the last meeting. Members confirmed that the revised text was acceptable and should be made available to members of the Expert Advisory Groups, Panels of Experts and Working Parties.

#### 887 **Application of ICH Disregard Limits** COM(14)31

Expert Advisory Group MC3: Medicinal Chemicals had discussed a monograph for which a manufacturer had requested inclusion of a lower disregard limit than that required by ICH guidelines for their validated method. The EAG had agreed, in principle, that the proposed disregard limit should be accepted as it reflected the sensitivity of the method; the inclusion of a higher limit (to be in line with ICH) could mean that the method was running at a less sensitive level. The EAG had also pointed out that the ICH limit was a minimum requirement and that the BP should not impose more stringent limits than ICH.

Members were invited to discuss whether (1) the ICH disregard limit should always be applied or (2) a degree of flexibility should be allowed to include a disregard limit in line with or lower than the ICH limit, depending on the method used. It was agreed that the preferred BP policy should be to follow the ICH guidelines, but that a flexible approach could be adopted, where justified, on a case-by-case basis.

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### VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

888 **Expert Advisory Groups, Panels of Experts and Working Parties: Review of Membership** COM(14)32

The term of office of all members of Expert Advisory Groups, Panels of Experts and Working Parties would expire on 31<sup>st</sup> December 2014. The Secretariat had reviewed the current membership of the various groups in consultation with relevant Chairs and Vice-Chairs in order to identify those members who should be retained and those who should be retired. Commission and EAG/Panel members had been invited to suggest potential candidate new members and a note had been included on the BP and MHRA websites inviting interested parties to provide a covering letter and CV to enable their suitability to be assessed. A list of the current membership of all the groups was provided, together with an indication of proposed new appointments, reappointments and retirements. The following points were drawn to the attention of members.

**EAG ULM: Unlicensed Medicines** Members endorsed the appointment of Dr Lee as Chair of EAG ULM.

**Panel VET: Veterinary Medicines** Members endorsed the appointment of Mr Coulson as Vice-Chair of the Panel.

**WP CX: Excipients** Members endorsed the recommendation to change the status of WP CX to that of a Panel of Experts, with Dr Matthews as Chair.

**WP AQbD: Analytical Quality by Design** Dr Steven Brown (Actavis) had been proposed as a representative from the British Generic Manufacturer's Association. Dr Brown's appointment had been endorsed by the Chair and Vice-Chair during the summer to enable him to attend the first meeting of the Working Party.

Members endorsed the proposed changes.

889 **EAG HCM Working Parties** COM(14)33

**Working Party DNA: Identification Techniques** Further to the discussions at the March 2014 meeting regarding the establishment of a Working Party to progress the work on developing molecular methods for inclusion in the British Pharmacopoeia, an informal meeting was held to discuss relevant issues (see minute 896). Terms of Reference for the new Working Party had been prepared and were accepted. A list of proposed members, including Dr Helliwell as Chair, was presented and endorsed.

**Working Party MCS: Microscopy** As a result of an informal meeting held in June to discuss issues relating to the microscopy part of the BP-NIBSC Herbal Project (minute 895 refers), it had been proposed that a Working Party should be established to progress the work. Members endorsed the establishment of the Working Party and the proposed members (including Professor Williamson as Chair).

890 **Expert Advisory Group ABS: Antibiotics** COM(14)34

The report of the EAG ABS meeting (18:02:14) was approved and the following points were raised.

**Work Programme** There was likely to be a shift towards the revision of older monographs as the resistance to certain newer antibiotics was resulting in the increased use of older products.

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**Sterile Amphotericin Concentrate** It was understood that liposomal products were available and that there might be a need to include monographs for both liposomal and non-liposomal forms. Advice would be sought before a monograph for a liposomal product was developed.

891 **Expert Advisory Group MC3: Medicinal Chemicals** COM(14)35

The report of the EAG MC3 meeting (25:02:14) was approved and the following point was raised.

**Revision of older monographs** The group had expressed concern at the delays in the revision of out-dated monographs but recognised the limited resources available.

892 **Expert Advisory Group PCY: Pharmacy** COM(14)36

The report of the EAG PCY meeting (10:03:14) was approved and the following points were raised.

**Dispensing Information in the BP** EAG PCY had discussed whether dispensing statements should be retained or removed and the recommendations would be provided to relevant EAGs for their input before any changes were made.

**Extemporaneous Preparations** The group had discussed whether those monographs that contained a formula and/or a method of preparation should be amended to open format or omitted in light of current usage information. The recommendations would be provided to relevant EAGs before any changes were made.

893 **Expert Advisory Group MC2: Medicinal Chemicals** COM(14)37

The report of the EAG MC2 meeting (22:05:14) was approved and the following points were raised.

**Aprepitant; Identification; Assay** A request to consider the use of identification by diode array detection, measuring the UV spectra from the Assay test and reference solutions, had been received. The group had recognised that not all laboratories would have this facility but agreed that the technique should be considered for inclusion in future BP methods.

**Sitagliptin Tablets** The draft monograph was being prepared in collaboration with the manufacturer and the USP, to enable prospective harmonisation.

894 **Expert Advisory Group MC1: Medicinal Chemicals** COM(14)38

The report of the EAG MC1 meeting (11:06:14) was approved and the following points were raised.

**Fenthion** The Veterinary Medicines Directorate had stated that Fenthion was no longer used in veterinary medicines in the UK and there were restrictions on its use as a pesticide within the European Union. Members endorsed the recommendation to omit the monograph from the next edition of the British Pharmacopoeia (Veterinary).

**Isoconazole Pessaries** Licensed products were no longer available and members endorsed the recommendation to omit the monograph from the next edition of the British Pharmacopoeia.

**Phenytoin Tablets; Related substances** A pre-washing of the TLC plate before carrying out the test had been found to be necessary in order to enable detection of the spots. This issue had not been reported for any other methods using fluorescent plates.

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- 895 **Informal Working Party: Microscopy** COM(14)39

The report of the informal microscopy meeting (24:06:14) was approved. Members were informed that the Secretariat was hoping to benefit from the expertise at NIBSC in modern microscopy techniques with a view to increasing and improving BP micrographs for herbal materials.

- 896 **Informal Working Party: DNA Bar-coding** COM(14)40

The report and summary report of the informal DNA bar-coding meeting (24:06:14) was approved. The intention was to develop a method that would ensure the material could be correctly identified and to carry this forward into the BP.

- 897 **Expert Advisory Group HCM: Herbal and Complementary Medicines** COM(14)41

The report of the EAG HCM meeting (25:06:14) was approved and the following point was raised.

**Golden Cinquefoil** Members endorsed the recommendation that the UK delegation should request that Golden Cinquefoil should be added to the work programme of the EP Commission to avoid duplication of work.

- 898 **Working Party AQbD: Analytical Quality by Design**

The first meeting of the AQbD Working Party had been held on 16 September 2014. There had been a lot of discussion on policy aspects, particularly around the Analytical Target Profile.

## VII EUROPEAN PHARMACOPOEIA

- 899 **European Pharmacopoeia Update** COM(14)42

**Pharmeuropa 26.3** A list of the draft documents in Pharmeuropa 26.3 was provided for information; comments were due by 30 September 2014.

**European Pharmacopoeia Commission** A copy of the Record of the 148<sup>th</sup> Session of the EP Commission (March 2014) was provided for information.

## VIII INTERNATIONAL COLLABORATION

- 900 **International Collaboration** COM(14)43

Members were provided with an update on international activities.

**Chinese Pharmacopoeia** A Memorandum of Understanding between the MHRA and the Chinese Food and Drug Administration was signed on 17 June 2014.

**Croatian Pharmacopoeia** The Croatian Agency for Medicinal Products and Medical Devices (“HALMED”) had requested permission to reproduce extracts from the BP relating to unlicensed medicines.

**Future meetings** Secretariat staff would be attending the following meetings in the next few months: EDQM 50<sup>th</sup> Anniversary Conference (Strasbourg, 6-8 October); WHO Fourth International Meeting of World Pharmacopoeias (Strasbourg, 8-10 October); 49<sup>th</sup> WHO Expert Committee Meeting (Geneva, 13-17 October); 59<sup>th</sup> WHO Meeting on International Non-proprietary Names (Geneva, 14-16 October); American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition (USA, November).

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**Informal Prospective Harmonisation with the USP** Three informally harmonised monographs under the remit of EAG MC2 had been published in the BP 2015.

### **IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR**

#### **901 British Pharmacopoeia's 150<sup>th</sup> Anniversary Event Week**

A report of the activities associated with the events to celebrate the 150<sup>th</sup> anniversary of the British Pharmacopoeia was provided for information.

#### **902 Strategy**

Commission would be provided with a summary of the strategy document at a future meeting.

#### **903 Tri-ennial Review**

The Department of Health would shortly be carrying out a Tri-ennial Review covering the work of the BP Commission, the Commission on Human Medicines and the MHRA.

#### **904 Appointments**

The Secretary and Scientific Director had raised concerns over the appointments process with the MHRA Corporate Executive Team, including apparent inconsistencies in the way the process was carried out for different organisations.

#### **905 Stakeholder Engagement**

Members of the Secretariat had attended a meeting of the European Federation of Pharmaceutical Industries and Associations (EFPIA) in July. Areas of mutual interest had been discussed, including harmonisation of standards, possible incentives to companies to support the BP and Good Pharmacopoeial Practices.

#### **906 Prioritisation of Monographs**

The Secretariat was reviewing the prioritisation of monographs, along with the review of the overall work programme.

### **X ANY OTHER BUSINESS**

#### **907 Date of next meeting**

Tuesday 16<sup>th</sup> December 2014.