

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 Tuesday 16th December 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, Dr B Matthews, Professor J Miller, Dr L Tsang, Mrs J M Turnbull.

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

Apologies for absence were received from Dr R Torano, Dr P Varley and Professor E Williamson.

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

Mr David Dipple, Ms Flora Goldhill and Mr Jamie Grant (Department of Health) also attended the meeting as observers.

908 **Introductory Remarks**

Welcome The Chair welcomed Mr Dipple, Ms Goldhill and Mr Grant to the meeting and noted that they were observing the meeting as part of the triennial review of the British Pharmacopoeia Commission.

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

909 The minutes of the meeting held on 22nd September 2014 were confirmed.

II MATTERS ARISING FROM THE MINUTES

910 The following matters arising from the meeting held on 22nd September 2014 were noted.

Minute 881 – BP Monographs for Herbs: Routine Inclusion of Assay Methods The EP Commission had been made aware of the EAG HCM and Commission discussions on this matter.

Minute 883 – BPCRS: User Guidance The Secretariat had held preliminary discussions with colleagues in the Inspectorate about this matter. Further discussions would be held and Commission would be updated at a future meeting.

Minute 886 – Aide Memoire The finalised Aide Memoire had been added to the BP website as agreed.

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III REPORTS AND CORRESPONDENCE

- 911 **British Pharmacopoeia Strategy: The Next 5 Years** COM(14)44

A document outlining the strategy for the British Pharmacopoeia operation over the next five years was provided for information.

- 912 **BP (Vet) Strategy: The Next 5 Years** COM(14)45

The Secretariat had started to develop a strategy for the British Pharmacopoeia (Veterinary) over the next five years. The intention was to ensure that the BP (Vet) continued to provide quality standards for veterinary medicines in the UK and overseas by increasing the number of monographs and increasing the extent to which the standards were applied.

Inclusion of BP (Vet) in Veterinary Medicines Regulations Members agreed that it was critically important for the BP (Vet) to be reinstated in the Regulations and it was noted that the Secretariat and the VMD were in discussion on this matter.

Panel VET vs EAG VET The remit of the current Panel of Experts focussed on policies relating to the development of monographs for veterinary medicines and the work programme; monographs were developed by the relevant Expert Advisory Groups.

Members agreed that it would be valuable to try and improve the number of veterinary monographs but were of the opinion that this could probably be achieved by increasing the number of veterinary experts on the current EAGs rather than establishing a separate EAG. After further discussion it was agreed that no change to the role or status of Panel VET should be made at this time and the group would continue to be invited to comment on proposed new BP (Vet) monographs.

- 913 **BP/NIBSC Biologicals Project** COM(14)46

The proposal to develop a secondary desmopressin reference standard had been discussed at the September meeting and a number of concerns had been raised.

Background and purpose EAG BIO had supported the development of the BP desmopressin reference standard. The methods in the draft formulation monographs were different from the method in the Ph Eur monograph for Desmopressin and development of a separate reference material suitable for carrying out the monograph tests was in accordance with BP policy. It had been confirmed that there was no prohibition on a secondary standard being generated from a WHO International Standard, since such standards were generally used to generate working standards rather than being used directly.

European Pharmacopoeia A master batch of primary reference standard would be retained by the EP Commission; any subsequent batches issued would be regarded as “secondary standards”. The policy of the EP (and the BP) was for reference standards to be supplied for immediate use; it was recognised that in many cases the industry would develop their own working standards, testing against the official standards.

- 914 **DNA Identification Techniques: Report** COM(14)47

BP-NIBSC Herbals Pilot The practical work on the DNA bar-coding project was in progress at NIBSC. The current intention was to publish a new Appendix providing general guidance on conducting DNA-based identification methods for herbal drugs in the BP 2016. Dr Helliwell praised the work of staff for their efforts and noted that the BP was the leading pharmacopoeia in this field.

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915 **BP Monographs for Anti-epileptic Drugs**

COM(14)48

Following the review of anti-epileptic drugs by the Commission on Human Medicines, it had been agreed that non-interchangeability statements should be included in monographs relating to category 1 and category 2 products in the British Pharmacopoeia 2016. The recommendations had been drawn to the attention of the Expert Advisory Group on Unlicensed Medicines and a number of issues had been raised.

Oral Solutions; Scope of CHM Recommendations EAG ULM had questioned whether a non-interchangeability statement was required for oral solutions since it was expected that solutions would be bio-equivalent. However, it had been pointed out that oral solutions were not necessarily interchangeable, particularly those containing sorbitol or other sugars. The members had also asked whether the recommendation related solely to oral dosage forms or to all formulations. It had been confirmed that the recommendations only related to oral drugs; they did not apply to parenteral formulations. It had also been confirmed that the recommendation applied to oral solutions since there was the potential for sorbitol to change the uptake of drugs with a narrow therapeutic range. The updated list of monographs that would be amended in the BP 2016 was provided for information. It was noted that a non-interchangeability statement would be appropriate for rectally-administered anti-epileptic drugs.

Monographs for Unlicensed Medicines EAG ULM had noted that it would be almost impossible to ensure that patients received the same unlicensed product during their course of treatment unless a fixed formulation was specified in the BP. Members had agreed that it was inappropriate to include non-interchangeability statements in monographs for unlicensed medicines. It had been proposed that, instead, a statement referring to the need to monitor patients receiving drugs with a narrow therapeutic index should be included.

It was agreed that the Secretariat should review the proposed wording in consultation with the Chair and Vice-Chair of EAG ULM and taking note of information in the BNF.

916 **E-Cigarettes: Update**

COM(14)49

In order to progress development of the new BP monograph for electronic (nicotine) cigarettes, the Secretariat of EAG MC1: Medicinal Chemicals had held a meeting with a representative from the British Standards Institute and relevant MHRA staff. The following issues had been discussed.

Publicly Available Specification vs British Standard A Publicly Available Specification (PAS) was a “sponsored fast-track standard driven by the needs of the client organisations and developed according to guidelines set out by the British Standards Institute”. PAS were non-mandatory, but after a period of two years they were reviewed to ascertain whether they should be progressed as British Standards.

BP Standard for e-Cigarettes A BP monograph would only apply to nicotine e-cigarettes that were above a certain strength and licensed as medicinal products in the UK and not to consumer (unlicensed, non-medicinal) products.

Draft PAS Comments on the draft PAS had been received from members of the Commission, EAG MC1 and the Pharmacy EAG. A copy of the consolidated comments sent to the BSI was provided for information; separate comments had been sent from the MHRA. The Chair thanked members for their input.

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917 **British Pharmacopoeia Laboratory** COM(14)50

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

IV FUTURE PUBLICATIONS

918 **Monograph Initiation: Candidate Monographs** COM(14)51

Monographs arising from the current Work Programme In accordance with the decision to elaborate monographs for all known formulations of a particular active ingredient, the following items had been identified as potential candidate monographs: Milbemycin and Lufenuron Tablets, Chewable Milbemycin and Praziquantel Tablets, Milbemycin and Praziquantel Tablets, Milbemycin and Spinosad Chewable Tablets. Commission endorsed the recommendation to add the items to the work programme.

Data Offered by Manufacturers A manufacturer of Valaciclovir Tablets had offered to provide data to support the development of a BP monograph and members endorsed the recommendation to add this item to the work programme.

2013 PCA Prescribing Data and CMU Hospital Pharmacy Data The Secretariat had examined the most recent lists of prescribed products provided by the NHS Information Centre and the Department of Health Commercial Medicines Unit. A number of items had been identified as potential candidate monographs from the top 500 most widely prescribed items and the top 100 items used in hospitals during 2013 and it was agreed that these should all be added to the work programme.

Future Identification of Candidate Monographs for Initiation The NHS Business Services Authority published quarterly data on the top 500 special order products. Recent data had been reviewed and presented to the Expert Advisory Group on Unlicensed Medicines. A number of items had been identified as potential candidate monographs for EAG ULM and the group had agreed that this offered a useful source of information to identify widely used unlicensed medicines.

919 **Approved Synonyms** COM(14)52

New Monographs Members confirmed that there was no need to create any approved synonyms as a consequence of new monographs added to the European Pharmacopoeia by means of Supplement 8.4 and recommended that the Ph Eur titles should be used when the monographs were reproduced in the BP 2016 and BP (Vet) 2016.

British Approved Names As a consequence of the new monograph for Zanamivir Hydrate an appropriate amendment would be made to the BAN entry for Zanamivir (anhydrous) to indicate that a monograph was included in the BP/Ph Eur, in accordance with current policy.

V ANALYTICAL ISSUES

None.

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VI EXPERT ADVISORY GROUPS / PANELS OF EXPERTS

- 920 **Expert Advisory Groups, Panels of Experts and Working Parties: Review of Membership** COM(14)53

In accordance with the decisions taken at the last meeting, letters had been sent to the proposed new members of EAGs/Panels and Working Parties and to those members who were to be re-appointed or had retired. An updated membership list would be provided at the next meeting.

Members noted the following changes that had occurred since the last meeting.

EAG ABS: Antibiotics Mr E Flahive (Elanco Animal Health) had confirmed that he would be willing to serve on EAG ABS in order to provide advice on veterinary medicines.

MHRA Representatives Mr David Deutsch had been proposed as a member of Panel CX: Excipients and Mr Geoff Lay had been proposed as a member of Panel IGC: Inorganic and General Chemicals. Members endorsed the appointments of Mr Deutsch and Mr Lay.

- 921 **Criteria for Appointment of EAG/Panel Members** COM(14)54

The Secretariat had prepared draft criteria to take into consideration when deciding whether to appoint/re-appoint members to the EAGs, Panels and Working Parties.

- 922 **Expert Advisory Group PCY: Pharmacy** COM(14)55

The report of the EAG PCY meeting (12:09:14) was approved and the following points were raised.

Monograph Structure Members had re-iterated their view that the inclusion of a first published/revised date in BP monographs would be useful.

Dissolution A member had raised an issue concerning the suitability of the basket method as it might not agitate the contents of the dissolution vessel sufficiently. However, it was noted that this was a harmonised text and so it could not be changed unilaterally.

- 923 **Working Party AQbD: Analytical Quality by Design** COM(14)56

The report of the first WP AQbD meeting (16:09:14) was approved. Members were informed that the BP was involved in a joint project which was currently the only pharmacopoeial application of QbD principles. The group included representatives from both innovator and generic pharmaceutical companies and members had provided an overview of their experiences to date. A widely used product had been chosen for inclusion in a BP/MHRA feasibility study and a number of issues had been identified.

- 924 **Expert Advisory Group MC3: Medicinal Chemicals** COM(14)57

The report of the EAG MC3 meeting (7:10:14) was approved and the following point was raised.

Alfacalcidol Capsules The use of chloroform was required; the only suitable alternative solvents were considered to be more toxic than chloroform and members had reluctantly agreed that, in this case, the use of chloroform should be permitted even though the policy was to avoid its use where possible. Commission supported the EAG's recommendation that if similar instances arose in the future chloroform should be used as a reagent.

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925 **Panel VIP: Veterinary Immunological Products** COM(14)58

The report of the Panel VIP meeting (13:10:14) was approved.

VII EUROPEAN PHARMACOPOEIA

926 **European Pharmacopoeia Update** COM(14)59

Pharmeuropa 26.4 A list of the draft documents in Pharmeuropa 26.4 was provided for information; comments were due by 31 December 2014.

European Pharmacopoeia Commission A copy of the Record of the 149th Session of the EP Commission (June 2014) was provided for information. At the 150th Session (November 2014), nominations for a number of new UK experts had been approved. Members were pleased to note that Professor Davidson had been elected as the Chair of the new Working Party on General Methods.

50th Anniversary of the European Pharmacopoeia Several members of the Secretariat and the Commission had attended the International Conference held in Strasbourg (“EDQM: 50 Years of Leadership in the Quality of Medicines – Paving the Way for the Future”) and had participated in a number of workshops at the event. A summary of the workshops and recommendations for the future was provided for information.

VIII INTERNATIONAL COLLABORATION

927 **International Collaboration** COM(14)60

Members were provided with an update on international activities.

Chinese Pharmacopoeia Mr Heddell (Director of Inspection, Enforcement and Standards, MHRA) and Dr Atkinson had attended the 7th Annual Joint Chinese Pharmacopoeia – USP Science and Standards Symposium and had given presentations on “Developing Pharmacopoeial Standards” and “Pharmacopoeial Harmonisation”. A meeting had been held with the Secretary General of the Chinese Pharmacopoeia to progress the co-operation between the two organisations, including development of a Memorandum of Understanding between the British and Chinese Pharmacopoeias.

Croatian Pharmacopoeia The draft co-operation arrangement with The Croatian Agency for Medicinal Products and Medical Devices had recently been approved by the Department of Health’s legal advisers and was nearing completion.

WHO 4th International Meeting of World Pharmacopoeias Mrs Vallender and Dr Swanson had attended this meeting which had been held in Strasbourg. The meeting had focussed on the continued development of the guidelines on Good Pharmacopoeial Practices.

Informal Prospective Harmonisation with the USP Work was continuing and the harmonisation project had been expanded to include a pilot study on a biological material and its product.

Staff had attended the following USP workshops: DNA Methods for Quality Control of Botanical Products; Lifecycle Approach to Validation of Analytical Procedures with Related Statistical Tools.

American Association of Pharmaceutical Scientists 2014 Annual Meeting and Exposition Mr Pound had attended this meeting on behalf of the BP and to support The Stationery Office’s efforts to increase the sales of the BP in the USA.

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Ghana Representatives from the Ghanaian Regulatory Authority had recently visited the MHRA. Mr Evans had given presentations on the Role of the BP and Nomenclature.

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

928 Herbal Drugs

The BP activities on herbal drugs had generated a lot of interest and the EDQM had expressed an interest in working with the BP in this area.

929 MHRA

Sir Michael Rawlins had taken up his post as Chair of the MHRA and would be invited to attend a future meeting of the BP Commission. The BP was working closely with the Communications Division and the intention was to send out a customer survey to UK and overseas users.

930 Meeting Papers

As part of a review of policies and procedures, the Secretariat had been looking at ways to improve the security of Commission/EAG/Panel documents.

Confidentiality Members were reminded that the proceedings of the BP Commission (and the EAGs, Panels and Working Parties) were confidential and that all material required for meetings should be retained/disposed of in a secure and confidential manner.

Electronic Working The MHRA had moved towards electronic working in recent years and the Secretariat proposed to trial electronic working within the BPC and EAGs/Panels for a period of one year. A number of concerns were raised and it was agreed that the Secretariat should give further consideration to the proposed move to electronic working before any changes were made.

931 Expenses

The expenses policy had been updated in line with the MHRA policy and had been provided to members.

X ANY OTHER BUSINESS

932 Medical Devices

A member drew attention to the fact that under the Medical Devices Directive official status was only granted to Ph Eur monographs if a reference to the relevant text was included in the Official Journal of the European Union and that, as far as he was aware, no such references had ever been published.

933 Annual Report

The 2014 Annual Report of the British Pharmacopoeia Commission would be provided to members during January for comment and approval.

934 BP Website

Members were provided with an update of the on-going work to combine and update the current BP website and the website providing the online version of the BP. The functionality of the current sites

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would be retained and improved and it was hoped that the new improved website would go live during the summer.

935 **Staff**

Members congratulated Dr Atkinson who had recently been appointed as Deputy Director of the Inspection, Enforcement and Standards Division of the MHRA.

936 **Date of next meeting**

Monday 30th March 2015.