

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 30th March 2015.

Present: Professor K Taylor (*Chair*), Professor D Cairns, Mr B J Capon (*Lay Member*), 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 R Torano, Dr L Tsang, Mrs J M Turnbull (*Lay Member*), Dr P Varley, Professor E Williamson.

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

An apology for absence was received from Professor A G Davidson (*Vice-Chair*).

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

937 **Introductory Remarks**

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

938 The minutes of the meeting held on 16th December 2014 were confirmed.

II MATTERS ARISING FROM THE MINUTES

939 The following matters arising from the meeting held on 16th December 2014 were noted.

Minute 930 – Electronic Working Further to the discussions at the last meeting, the Secretariat had sent out a survey seeking views on the proposed move to electronic working. A range of responses had been received and would be reviewed by the Secretariat.

Minute 933 – Annual Report The Annual Report had been finalised and would be published as part of the Medicines Advisory Bodies Reports later in the year.

III REPORTS AND CORRESPONDENCE

940 **British Pharmacopoeia – NIBSC Herbal Project** COM(15)1

A report was received from the Chair of the Working Party on Identification Techniques (DNA) which provided a summary of the work carried out over the last 12 months on the joint BP – NIBSC Herbal Project.

941 **Inhaled Products** COM(15)2

Policy The former Working Party on Inhaled Products had made a number of recommendations which had been formalised in a policy document which had been included on the BP website. A

British Pharmacopoeia Commission

number of changes to the recommendations had subsequently been discussed by the Expert Advisory Group on Pharmacy and a revised policy document (“British Pharmacopoeia Monographs for Inhaled Products”) had been prepared.

Members endorsed the revised policy document and agreed that it should be included on the website. The changes would be brought to the attention of relevant Expert Advisory Groups and affected monographs would be amended in a future publication.

Supplementary Chapter I O: Inhaled Products The Supplementary Chapter, which had been withdrawn from the BP 2015, had been revised to reflect the contents of the updated policy document and to ensure consistency with Licensing requirements. The revised Chapter was accepted and would be included in the BP 2016.

942 **British Pharmacopoeia Laboratory** COM(15)3

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

Proficiency Testing The Laboratory had participated in a number of Proficiency Testing studies in recent years. This was as part of a wider testing activity of the Laboratory of the Government Chemist (LGC); both the MHRA and the BP Laboratories had been involved in a number of studies which had been run by the EDQM.

943 **British Pharmacopoeia Alternative Technology** COM(15)4

The Secretariat had been considering ways to increase the BP portfolio of products (hard copy, online, USB). It was agreed that Commission should be kept informed of developments.

944 **BP Publications: Future Requirements** COM(15)5

The current publication contract with The Stationery Office (TSO) would expire following publication of the BP 2017. The MHRA had initiated the early stages of the publication contract tender process and a Prior Information Notice had been issued which described the contract that would be advertised in the near future.

Members were invited to consider future publication requirements and to propose any novel or innovative ideas that could be incorporated within the next contract.

IV FUTURE PUBLICATIONS

945 **British Pharmacopoeia 2016 Publications** COM(15)6

BP 2016 The Secretariat was currently preparing text for inclusion in the British Pharmacopoeia 2016 and the British Pharmacopoeia (Veterinary) 2016. All items included in the eighth edition of the European Pharmacopoeia, together with those from Supplements 8.1 to 8.5, would be incorporated in either the BP 2016 or the BP (Vet) 2016, as appropriate. The 2016 publications would be published in August 2015 and would come into effect on 1st January 2016.

British Pharmacopoeia Commission

Electronic updates The text from Supplement 8.3 had been added to the online BP to coincide with implementation of the Supplement on 1st January 2015. Text from Supplements 8.4 and 8.5 would be available on the online BP from 1st April and 1st July respectively.

Text for approval The first batch of new and technically revised monographs for the BP 2016 publications had been reviewed by members during February. It was intended that the final batch of text would be posted on the BP website on **8th April**, with a deadline for comment of **22nd April**.

Preliminaries Members recommended that the British Pharmacopoeia 2016 and the British Pharmacopoeia (Veterinary) 2016 should be published and confirmed that the draft Prefaces to both publications were acceptable.

Technical / Editorial Changes

Chloroform; Chloroform-containing Preparations In accordance with the discussions regarding the removal of chloroform as an ingredient from UK marketed products, the previously agreed changes would be included in the BP 2016 (omission of monograph or removal of formula and/or method of extemporaneous preparation). In addition, a statement would be added to the General Monograph on Unlicensed Medicines recommending that the use of chloroform as an ingredient in unlicensed medicines should be avoided.

Anti-epileptic Preparations The previously agreed non-interchangeability statements would be added to the affected monographs in the BP 2016.

946 **Monographs for Omission from the BP 2016 and BP (Vet) 2016** COM(15)7

Since publication of the BP 2015 publications, a number of monographs had been identified as candidates for omission from the BP 2016 publications. Members endorsed the recommendation to omit these monographs from the BP 2016 and the BP (Vet) 2016. In accordance with regulation 252 (2c) of the Human Medicines Regulations 2012, these monographs would continue to remain in force.

947 **Approved Synonyms** COM(15)8

New Monographs The draft list containing one new Approved Synonym relating to items added to the European Pharmacopoeia by means of Supplement 8.5 was approved. The item 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.

British Approved Names As a consequence of additions to the Ph Eur, **Macrogol Isotridecyl Ether** would be added as a new British Approved Name in a future BAN publication.

948 **British Approved Names 2012: Supplement No. 4** COM(15)9

Supplement No. 4 to British Approved Names 2012 had been prepared and approved by the EAG on Nomenclature, subject to a number of changes to the Action and use statements. All the entries were either recommended International Nonproprietary Names (rINN) which had UK product licences or were Ph Eur monograph titles which had previously been approved for inclusion in the list of BANs.

In accordance with established practice, the list of amendments included the BAN entry in full. It was suggested that it would be helpful to the user to identify what had been changed in the amended entries and the Secretariat agreed to examine whether this approach could be incorporated in future publications. Subject to any comments received by **13th April**, the Commission approved the content of the draft Supplement and recommended that it should be published.

British Pharmacopoeia Commission

949 **Monograph Initiation: Candidate Monographs** COM(15)10

Monographs arising from the current Work Programme Members endorsed the proposal to add Azithromycin Eye Drops and Azithromycin Powder for Infusion to the work programme. This would enable five Azithromycin formulation monographs to be developed as a family.

International Pharmacopoeia Members endorsed the proposal to add Moxifloxacin Tablets to the work programme. Although a low use product, the item met the criterion for developing family monographs. The monograph was also on the work programme of the WHO International Pharmacopoeia and the intention was to provide a harmonised monograph that could be included in both the BP and the IP.

Informal Harmonisation Merck had requested that a harmonised monograph for Fosaprepitant Dimeglumine Powder for Solution for Infusion be developed between the BP and the USP and members endorsed the proposal to add the item to the work programme.

950 **Monograph Lifecycle Review: Omissions** COM(15)11

The Secretariat was currently reviewing the processes and prioritisation involved in the initiation, development, publication and revision of monographs.

Absence of Licensed Products A review of low-selling BPCRS had identified a number of materials used in monographs for which licensed products were no longer available in the UK.

Omission of Monographs The current policy was that if licensed products were no longer available in the UK, and the items were not used in countries that included the BP in their legislation, the monograph would be omitted from the BP or BP (Vet).

Proposed Action In light of the potentially large number of monographs for items that were no longer used, and to avoid establishing and re-testing BPCRS that were no longer required, the Secretariat had recommended that a formal review process should be developed.

Whilst members were generally supportive of the proposals, a number of concerns were raised including: the potential omission of monographs that were used in other countries; the fact that pharmacopoeial methods should be “simple” and should avoid the use of equipment that was not universally available.

After further discussion, Commission endorsed the proposed review process.

V ANALYTICAL ISSUES

951 **Analytical Methods – Evaluation Assessment** COM(15)12

Current Situation The extent of laboratory evaluation required for a new or revised analytical method was considered during the elaboration or revision of a monograph by the relevant Expert Advisory Group. This could result in laboratory evaluation of methods or inclusion of a manufacturer’s validated method without laboratory checking (arm-chairing monographs). EAG MC2 (Medicinal Chemicals) had suggested that a formal documented assessment should be recorded when methods were adopted without laboratory evaluation in order to ensure that a consistent approach was adopted across all the EAGs.

Members agreed that it would be valuable to adopt a formalised approach and that the proposals should be trialled for the autumn round of meetings. It was also agreed that further guidance should

British Pharmacopoeia Commission

be provided to experts, including real examples, to ensure that EAG and Panel members become familiar with the process.

952 **Prolonged-release Preparations: Dissolution Testing** COM(15)13

A joint project between the BP/MHRA and the University of Reading was in progress to examine the feasibility of developing a standard dissolution test that could be applied to prolonged-release preparations. The current policy was that reference to the dissolution of such preparations was included in a Production statement rather than in a mandatory test.

Members agreed that including a test and limits would be preferable to the current Production statement approach or the USP approach of including more than one dissolution test in a monograph. However, the consensus was that it would be very difficult to develop a standard test and limits in view of the differences in the formulations and the different release profiles. Commission would be kept informed of developments.

VI **EXPERT ADVISORY GROUPS / PANELS OF EXPERTS**

953 **Expert Advisory Groups, Panels of Experts and Working Parties** COM(15)14

An updated list of members, incorporating all the newly appointed members, was provided for information.

Panel VET: Veterinary Medicines Professor Peter Lees had decided to retire from the Panel. Mr Coulson and Professor Williamson paid tribute to the contributions Professor Lees had made in the field of veterinary medicine and to the Panel and noted that he would be very difficult to replace. A letter of thanks for his past service had been sent.

New Appointments Members endorsed the following additional appointments:

EAG NOM: Nomenclature Ms Belen Granell-Villen (Clinical Writer, British National Formulary);

EAG PCY: Pharmacy Professor Stephen Wicks (Professor in Pharmaceutical Sciences, University of Greenwich);

Panel MIC: Microbiology Dr Brian Alexander (Regulatory Compliance Manager, Scottish National Blood Transfusion Service);

Working Party DNA: Identification Techniques Dr Ian Feavers (Head of Bacteriology, NIBSC).

954 **Criteria for Appointment of EAG/Panel Members – Updated** COM(15)15

The draft criteria for appointment and re-appointment to the Expert Advisory Groups, Panels of Experts and Working Parties had been amended in accordance with the decisions taken at the last meeting. The revised document was accepted. It was intended to circulate the criteria to all existing members for information and to publish the criteria for **new** appointments on the BP website in due course.

955 **Expert Advisory Group ULM: Unlicensed Medicines** COM(15)16

The report of the EAG ULM meeting (4:11:14) was approved and the following points were raised.

Dispensing and Supply Statements EAG ULM had considered the recommendations from EAG PCY regarding the dispensing and supply statements in the monographs for Sodium Bicarbonate Oral Solution and Sodium Chloride Oral Solution. It had been agreed that to avoid any confusion

British Pharmacopoeia Commission

about the strengths available, the current statements should be retained with minor editorial amendments.

Monographs for Anti-epileptic Drugs Further to the discussion at the December meeting about the proposed patient monitoring statement for inclusion in the monograph for Paediatric Phenobarbital Oral Solution (minute 915 refers), the following statement had been agreed by the Chair, Vice-Chair and MHRA representatives on EAG ULM:

“Different formulations of Paediatric Phenobarbital Oral Solution may vary in bioavailability. Patients should be monitored to ensure blood levels remain within the required therapeutic range.”

Members agreed that the proposed statement was acceptable and that it adequately addressed the concerns raised previously.

Parenteral Nutrition Solutions The Group had previously agreed that it would be helpful to provide some guidance on Parenteral Nutrition Solutions. It had subsequently been agreed that the guidance should form part of a wider Supplementary Chapter on Aseptic Preparations. A first draft had been presented to EAG ULM and an updated text would be provided to Commission at a future meeting.

956 **Expert Advisory Group BIO: Biological and Biotechnological Products** COM(15)17

The report of the EAG BIO meeting (6:11:14) was approved and the following points were raised.

Bacterial Endotoxin Testing – BP Policy EAG BIO had endorsed the proposed policy on Bacterial endotoxin testing that had been considered at the March 2014 meeting (minute 853 refers). In addition EAG BIO had recommended that: (1) for new BP monographs where the use of a specific method was required the method should be included in the monograph, but without a limit and (2) for existing monographs that included a test and limit, no changes should be made.

Desmopressin Oral Powder It was confirmed that the test for Uniformity of dosage units should be included rather than that for Uniformity of content. The EAG had discussed the concerns raised by the Commission regarding the proposed development of a secondary desmopressin reference standard and further aspects had been discussed with NIBSC. It had been agreed that work on the pilot study to develop the secondary reference standard should continue but this would be kept under close review.

957 **Expert Advisory Group MC2: Medicinal Chemicals** COM(15)18

The report of the EAG MC2 meeting (20:11:14) was approved and the following points were raised.

Aprepitant Capsules; Identification It was noted that an increasing number of companies were using HPLC with diode array detection as a means of both identifying and quantifying materials. It was intended to present a paper on this at a future meeting.

Adrenaline and Noradrenaline Preparations The MHRA Laboratory was examining the Adrenaline and Noradrenaline preparations with a view to updating the monographs.

Alendronic Acid Tablets Problems had been reported with the published Related substances test, which had been arm-chaired. Laboratory work had been carried out and a revised method would be included in the BP 2016.

British Pharmacopoeia Commission

958 **Expert Advisory Group MC1: Medicinal Chemicals** COM(15)19

The report of the EAG MC1 meeting (15:12:14) was approved and the following points were raised. Dr Herbert Schmidt (International Pharmacopoeia, WHO) had attended the meeting as an observer as part of a visit to learn about the working practices of the BP.

Prolonged-release Sodium Valproate Capsules & Tablets It had been noted that there was a conflict between the wording of the established non-interchangeability statement for prolonged-release formulations and the statement recently agreed for inclusion in monographs for anti-epileptic drugs. It had been agreed that for any affected prolonged-release anti-epileptic oral dosage forms, the prolonged-release statement should be included.

Fluconazole Capsules Data provided by the International Pharmacopoeia had been used as a basis for this draft monograph.

Zidovudine Infusion; Content of zidovudine It was questioned whether the proposed content limits (95.0 to 105.0%) were appropriate in light of the proposed impurity limits. The Secretariat said that the limits had been supported by batch data and undertook to confirm the limits with the manufacturer before finalising the monograph.

959 **Expert Advisory Group PCY: Pharmacy** COM(15)20

The report of the EAG PCY meeting (2:2:15) was approved and the following points were raised.

Report of Group 12: Eye Preparations A proposal to include limits for sub-visible particles in the general monograph for Eye Preparations would be included in a future issue of Pharmeuropa. The value of such a test was questioned since the eye was always exposed to particulate matter, but it was pointed out that the test would serve as an indicator of compliance (or otherwise) with good manufacturing practices.

General Monographs for Pharmaceutical Dosage Forms Members were informed that Ph Eur Group 12 were reviewing a number of general monographs for dosage forms. It had been agreed that a number of further changes should be requested as a consequence of the Ph Eur proposal to refer to the general monograph for Pharmaceutical Preparations in all general monographs for dosage forms.

960 **Expert Advisory Group MC3: Medicinal Chemicals** COM(15)21

The report of the EAG MC3 meeting (25:2:15) was approved and the following point was raised.

Dispensing and Supply Statements EAG MC3 had welcomed and endorsed the proposals from EAG PCY to remove dispensing and supply statements from a number of monographs.

VII EUROPEAN PHARMACOPOEIA

961 **European Pharmacopoeia Update** COM(15)22

Pharmeuropa 27.1 A list of the draft documents in Pharmeuropa 27.1 was provided for information; comments were due by 31 March 2015.

European Pharmacopoeia Commission A copy of the Record of the 150th Session of the EP Commission (November 2014) was available on the BP website. A summary of the decisions taken at the 151st Session (March 2015) was provided at the meeting.

British Pharmacopoeia Commission

VIII INTERNATIONAL COLLABORATION

962 International Collaboration

COM(15)23

Members were provided with an update on international activities.

Chinese Pharmacopoeia The Memorandum of Understanding between the MHRA and the Chinese Pharmacopoeia had not yet been finalised. Dr Atkinson and Mr Evans had attended a meeting with China Britain Business Council (CBBC) to discuss promotion of the BP in China in collaboration with The Stationery Office.

Croatian Pharmacopoeia The Co-operation Agreement between the MHRA and the Croatian Agency for Medicinal Products and Medical Devices permitting the inclusion of BP text relating to unlicensed medicines in the Croatian Pharmacopoeia had been signed in February.

United States Pharmacopoeia Dr Ron Piervincenzi and Dr Tina Morris (USP) had met with Mr Heddell and several members of the Secretariat in February. Updates on collaboration activities, including BP and USP collaboration on biological materials, were provided at the meeting and the BP had been informed of forthcoming USP activities.

Future activities Staff would be attending the following meetings over the next few months: WHO Consultations on Specifications for Medicines, Sampling and Technologies (Geneva); WHO Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances (Geneva); WHO 5th International Meeting of World Pharmacopoeias (Washington DC); USP Convention (Washington DC).

IX REPORTS OF THE SECRETARY AND SCIENTIFIC DIRECTOR

963 Digital Work Place

It was noted that the MHRA would be updating its IT infrastructure over the next few years with a view to increased electronic working.

964 BP Website

Members were informed that good progress was being made on the development of the new consolidated BP website and that it was intended to launch the site at the same time as the BP 2016 publications. The building phase was almost complete and a number of testing phases to check both the content and functionality would be carried out. Mr Gibb said he hoped that a number of BP experts would assist in the testing phase and asked members to let him know if they would be willing to be involved in the process. The content of the existing BP website had been updated in line with government guidelines on writing for websites and should be more useful and accessible.

965 Triennial Review

The Triennial Review of the BP Commission had been completed and the report was now publicly available. Dr Atkinson thanked those members who had been involved in the process. The outcome of the review had been that the functions of the BP Commission were still required and that the Commission should be retained as an advisory Non-Departmental Public Body. The review had included a number of recommendations that would need to be addressed in the coming months.

British Pharmacopoeia Commission

X ANY OTHER BUSINESS

966 MHRA Website

In line with the websites of all government departments and agencies, the MHRA website had recently been merged into a single government site (www.gov.uk); the BP had been exempted from the requirement to move to gov.uk and had been allowed to retain its separate website. Several members commented that it was now extremely difficult to find relevant information relating to the MHRA. Dr Atkinson asked members to put their comments in writing so that they could be raised through appropriate channels.

967 Appraisals

The appraisals for members would shortly be carried out by telephone conversation.

968 Staff

Mrs Matilda Vallender would be retiring from the BP at the end of May after 35 years of service and the Chair paid tribute to her contribution to the work of the BP over the years. Mrs Vallender said that it had been a privilege to work in the organisation and wished her successor well.

969 Date of next meeting

Monday 6th July 2015.