BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group ULM: Unlicensed Medicines

SUMMARY MINUTES

A meeting of the Expert Advisory Group on Unlicensed Medicines was held at 151 Buckingham Palace Road, London, SW1W 9SZ on Monday 23rd April 2018.

Present: Dr M G Lee (*Chair*), Mr V Fenton-May (*Vice-Chair*), Mr D Caulfield, Ms S Hartley, Dr S Ho, Mr M Santillo, Dr J Smith, Mr A Sully and Mr P Weir.

In attendance: Dr F J Swanson, Mr P Crowley, Mr S Young, Ms M Rueda.

Apologies for absence were received from Dr S Branch, Mr W Goddard and Mr J Rickard.

508 **Introductory Remarks**

Welcome; Membership The Chair welcomed Dr Ho and Ms Rueda, who were attending their first meeting.

Relocation of the MHRA The move to the new offices for the MHRA had been tentatively scheduled to take place over three weekends beginning on 15th June. The new address would be: MHRA, 10th Floor, 10 South Colonnade, Canary Wharf, London E14 4PU. The existing phone numbers and email addresses would remain the same.

Travel and Expenses Members were reminded that any queries with regard to travel arrangements or expenses should be sent to Mr Brian Delahunty at the Secretariat.

Declaration of Interests Members were reminded to declare specific interests as they arose during the meeting and to inform the Secretariat of any changes to their interests throughout the year.

I MINUTES

509 The minutes of the meeting held on 17th October 2017 were confirmed.

II MATTERS ARISING FROM THE MINUTES

510 The following matters arising from the meeting held on 17th October 2017 were noted.

Minute 483 – Membership Dr Sze Man Ho (Pharmaceutical Assessor) had been appointed as a temporary replacement member from the Licensing Division.

Minute 496 – Lorazepam Oral Suspension In the absences of any information on the control of impurities, the monograph would be published in the BP 2019 without a Related substances test.

Minute 497 – Nadolol Oral Suspension; Minute 498 – Nifedipine Oral Suspension Further work on these items would be undertaken during the summer and reports should be available at the next meeting.

III REPORTS AND CORRESPONDENCE

511 British Pharmacopoeia 2019 ULM(18)1

The Secretariat was currently heavily involved in the production of the British Pharmacopoeia 2019, which would be published in August and would come into effect on 1st January 2019. The BP 2019 would contain all of the text from the 9th edition of the European Pharmacopoeia, together with that from Supplements 9.1 to 9.5. Updates to the online version of the BP 2019 would be made during the year, adding the text of further Ph Eur Supplements. A list of the new and revised texts that were the responsibility of this EAG that would be published in the BP 2019 had been provided for information.

Ketamine Nasal Spray; Potassium Acetate Sterile Concentrate The Expert Advisory Group on Nomenclature had confirmed that the proposed Action and use statements for these monographs were acceptable.

Ciclosporin Eye Drops A licensed product was now available and unlicensed formulations were no longer prepared. In accordance with current practice the responsibility for the monograph would be transferred to the relevant Expert Advisory Group (ABS: Antibiotics) and the ULM opening statement and reference to the General Monograph for Unlicensed Medicines would be removed by means of the BP 2019.

512 Extemporaneous Preparations ULM(18)2

At the last meeting a reduced set of criteria for deciding whether extemporaneous preparation details should be retained in a monograph or moved to a Supplementary Chapter had been discussed. The matter had been further discussed between the Secretariat of this EAG and that of the Expert Advisory Group on Pharmacy prior to the most recent meeting of EAG PCY. The approach had been refined and a decision tree had been designed which was intended for use by all the EAGs when reviewing their monographs.

513 Dispensing and Supply Statements ULM(18)3

There were currently a number of BP monographs which contained statements in the form: "*When [product name] is prescribed or demanded, [monograph title] shall be dispensed or supplied*." As information on prescribing is not within the remit of the BP, and as some of the statements might not reflect current practices, the Expert Advisory Group on Pharmacy had recently undertaken a consultation to ascertain whether these statements should be retained or removed from the affected monographs.

A public consultation had been held between December 2016 and January 2017 and the majority of responses had supported removing dispensing and supply statements from the BP. The matter had been discussed by the BP Commission in November 2017 and the Commission had endorsed the EAG PCY recommendation to remove all the statements from a future edition of the BP, subject to confirmation from the Department of Health.

514 Monograph Titles ULM(18)4

The British Pharmacopoeia Commission had recently endorsed a recommendation arising from the Pharmacy EAG to update monograph titles where the standard term was split (eg. Prolonged-release ACTIVE Tablets) to reflect the current regulatory requirements for naming medicines. This would result in monograph titles where the standard term was no longer split (eg. ACTIVE Prolonged-release Tablets). It had been agreed that this approach should be adopted for new monographs published in the BP 2019 onwards and that all currently affected monographs should be updated over the next five years.

515 **Intraocular Injections** ULM(18)5

The draft Supplementary Chapter and General Monograph for Intraocular Injections had been presented to the BP Commission at their March meeting. The Commission had endorsed publication of the texts in the BP 2019, subject to minor editorial amendments.

516 **Reconstituted Intravenous Preparations** ULM(18)6

A proposal from the Chair was presented regarding the provision of information on the preparation and stability of reconstituted intravenous additive preparations within the BP.

It had previously been agreed to expand the Supplementary Chapter on the Aseptic Preparation of Unlicensed Medicines to include a section on IV additives and the inclusion of non-mandatory information on the preparation and stability of such preparations could be valuable to users.

Dr Lee had started to prepare general text relating to IV additives for inclusion in Supplementary Chapter V F and he agreed to continue this with a view to presentation at the next meeting.

517 **Membership Review** ULM(18)7

The term of office of all members of BP Expert Advisory Groups, Panels of Experts and Working Parties would expire on 31st December 2018 and a comprehensive review of membership would be undertaken in the second half of the year. Members were asked to suggest potential candidate new members, taking note of the duties of a member (as detailed in the BP) and the criteria for appointment and re-appointment.

IV NEW MONOGRAPHS

518 **Work Programme** ULM(18)8

Revised format The Secretariat had recently consolidated the work programmes of all the individual Expert Advisory Groups into a format that enabled reports to be generated on current monographs in development and those under revision. The main and secondary work programmes of EAG ULM had been consolidated and incorporated within the overall work programme. The information relating to ULM monographs was provided for information, including the details of those members who had previously offered to provide assistance in developing monographs. It was noted that the work programme changed over time and the revised format made it easier to keep up-to-date.

Review At the last meeting it had been noted that many items had been on the work programme for a considerable time and that a comprehensive review should be undertaken in order to produce a more relevant and realistic list of monographs. Members endorsed the following proposed course of action:

(i) review items on the list to see if any are licensed and move to relevant EAG if appropriate;

(ii) review items on the list against recent hospital usage and prescription data and prioritise accordingly or remove from the list if no usage indicated;

(iii) identify collaborating partners to assist in monograph development (eg. EAG member, BP Laboratory, etc.).

Additions Data had been obtained relating to items prescribed during 2017. The Secretariat intended to review the data with a view to identifying any potential items to add to

the work programme. Members were invited to propose further additions and buffered antibiotics were identified as a key group of products.

519 **Naltrexone Capsules** ULM(18)9

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

V MONOGRAPHS IN PROGRESS

520 **Diltiazem Oral Suspension** ULM(18)10

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

521 **Ferric Chloride Injection** ULM(18)11

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

522 **Metoprolol Oral Suspension** ULM(18)12

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

523 **Parenteral Nutrition Solutions** ULM(18)13

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

524 **Carvedilol Oral Suspension** ULM(18)20

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

525 **Clomipramine Oral Suspension** ULM(18)21

The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

VI REVISION OF MONOGRAPHS

526 **Format of EAG ULM Monographs** ULM(18)14

Current format The current approach for monographs developed by this EAG was to include reference to the unlicensed status of the formulation at the head of the monograph and a reference to the General Monograph for Unlicensed Medicines in the italicised statement following the definition. There had been a few instances where licensed products had become available and the monograph had been transferred to the relevant Expert Advisory Group following removal of the opening statement and modification of the italic statement.

Proposed new format In view of possible delays in updating monographs the Secretariat had proposed a number of minor changes that should avoid the immediate need to update monographs and would prevent potentially inaccurate statements being published.

Opening statement It was agreed that the statement at the head of the monograph should be amended to read "NOTE: *This monograph was developed to cover unlicensed formulations*".

General Monograph statement It was agreed that cross-reference to the appropriate General Monographs should be amended to read: "*The [injection / oral solution, etc.] complies with the requirements stated under [Parenteral Preparations / Oral Liquids, etc.] and with the following requirements. Where appropriate, the [injection / oral solution, etc.] also complies with the requirements stated under Unlicensed Medicines.*"

It was agreed that the proposed change in approach should be adopted for new EAG ULM monographs and that current monographs should be updated at the earliest opportunity.

527 **Chloral Hydrate Oral Solution** ULM(18)15

Formulations available The Secretariat had become aware of a licensed product and so the opening statement relating to the unlicensed status would be removed from the monograph. According to the BNF the product was also available from Special Order Manufacturers. In light of the preceding discussion on the format of monographs (minute 526 refers), it was agreed that the General Monograph cross-reference should be amended to reflect that both licensed and unlicensed formulations were available.

Chloral Mixture; Paediatric Chloral Mixture The BNF included a reference to "Chloral Mixture, BP 2000" and included a method of extemporaneous preparation that was not exactly in accordance with the method specified in the BP 2000. It was agreed that the Secretariat should contact the BNF and request amendment of the entry to reflect the BP 2000 text.

528 **Moxifloxacin Intracameral Injection** ULM(18)16

Identification The Laboratory had undertaken further practical work in order to try and improve the proposed TLC identification test. Improved chromatography had been obtained by diluting the test and reference solutions to contain 0.004% w/v of Moxifloxacin Hydrochloride and by using methanol as diluent. The modified conditions had been incorporated in the revised monograph that would be included in the BP 2019.

529 **Sterile Silver Nitrate Solution** ULM(18)17

The current monograph for Sterile Silver Nitrate Solution covered products that could either be used as a cutaneous solution, an irrigation solution or an ophthalmic solution. If the text was developed today, the approach would be to include separate monographs due to the different General Monograph and Labelling requirements. Members agreed that it would be useful to split the monograph to reflect the different uses, depending on what was available. There was also a published monograph for Silver Nitrate Solution (non-sterile cutaneous solution). The Secretariat would try and obtain more information on the use and availability of these formulations with a view to providing revised texts at the next meeting.

VII INTERNATIONAL

530 Paediatric Formulary Working Party ULM(18)18

The reports of the 7th and 8th meetings of the Paediatric Formulary Working Party were provided for information.

531 International Activities ULM(18)19

Co-operation Agreement with Croatia The agreement between the MHRA (BP) and HALMED (the Croatian Agency for Medicinal Products and Medical Devices), permitting the translation and inclusion of the BP General Monograph and Supplementary Chapters on Unlicensed Medicines in the Croatian Pharmacopoeia, had been extended until February 2021.

Good Pharmacopoeial Practices: Compounded Preparations The draft guidance on Compounded Preparations had been accepted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations. The BP had provided editorial assistance in finalising the text which was expected to be included within the main Good Pharmacopoeial Practices document in the near future.

VIII ANY OTHER BUSINESS

532 Sterility of Extemporaneous Preparations

The pharmacopoeial test for sterility was based on statistical results obtained on batches and it was recognised that the production of batches and the required level of sampling was not feasible for one-off or extemporaneously prepared items.

Members agreed that it would be useful to include a form of “get-out clause” relating to such preparations in the BP and Mr Fenton-May agreed to try and progress this through his roles as Chair of the BP Panel of Experts on Microbiology and the Ph Eur Group of Experts on Biological Methods and Statistical Analysis. Members were invited to send any comments on this issue to Mr Fenton-May directly.

533 Date of next meeting

Monday 15th October 2018.