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 Tuesday 25th April 2017.

Present: Dr M G Lee (*Chair*), Mr V Fenton-May (*Vice-Chair*), Mr W Goddard, Ms S Hartley, Dr N Hussain, Mr J Rickard, Mr M Santillo, Dr J Smith, Mr A Sully, Mr P Weir and Dr M Westwood.

In attendance: Dr F J Swanson, Mr P Crowley, Mr S Young, Ms F Lee and Ms C Galdino.

Apologies for absence were received from Dr S Branch and Mr D Caulfield.

457 **Introductory Remarks**

Welcome The Chair welcomed members to the meeting. A special welcome was extended to Ms Sarah Hartley (Manager of Analytical Research and Development, Rosemont/Perrigo), a new member who was attending her first meeting.

Email addresses All email addresses for BP and MHRA staff had changed during April and were now in the format firstname.surname@mhra.gov.uk.

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

458 The minutes of the meeting held on 20th October 2016 were confirmed.

II MATTERS ARISING FROM THE MINUTES

459 The following matters arising from the meeting held on 20th October 2016 were noted.

Minute 428 – Moxifloxacin Intracameral Injection A supplier had agreed to provide a sample, which should enable the outstanding practical work to be carried out before the next meeting.

Minute 439 – Nadolol Oral Suspension; Minute 440 – Nifedipine Oral Suspension A member had arranged for practical evaluation of these monographs to be undertaken by university students. It was hoped that the work would be completed in time for presentation at the next meeting.

Minute 442 – Diltiazem Oral Suspension The Laboratory evaluation would be undertaken later in the year, pending receipt of samples.

Minute 444 – Metoprolol Oral Suspension The Laboratory evaluation would be undertaken later in the year, pending receipt of samples.

Minute 446 - Hydroquinone The practical evaluation of the IR and TLC identification tests would be carried out shortly and a report would be presented at a future meeting.

III REPORTS AND CORRESPONDENCE

460 **Membership** ULM(17)1

It had previously been agreed that suitable members from the Specials industry should be appointed to EAG ULM and members were pleased to note the appointment of Ms Hartley (Rosemont). The Secretariat would continue to try and identify suitable additional members.

461 **British Pharmacopoeia 2018** ULM(17)2

The Secretariat was currently heavily involved in the production of the British Pharmacopoeia 2018, which would be published in August and would come into effect on 1st January 2018. The BP 2018 would contain all of the text from the 9th edition of the European Pharmacopoeia, together with that from Supplements 9.1 and 9.2. Updates to the online version of the BP 2018 would be made during the year, adding the text of further Ph Eur Supplements. A list of the 6 new monographs and the revised texts that were the responsibility of this EAG that would be published in the BP 2018 had been provided for information.

Tretinoin, Hydrocortisone and Hydroquinone Cream The Expert Advisory Group on Nomeclature had recommended inclusion of the following action and use statement: Vitamin A analogue (retinoid) + corticosteroid + depigmenting agent. This was in line with the approach for other products containing two or more active ingredients and was accepted.

Phenylephrine Intracameral Injection Comments had been received from a supplier confirming that the new Related substances test, including the limits, was suitable for their product.

462 **Issues Arising through the BP Commission** ULM(17)3

New Analytical Techniques The BP Commission had recently agreed to establish an *ad-hoc* group whose objective would be to consider how the BP could best respond to the increased use of new analytical technologies whilst maintaining the pharmacopoeial approach of including established techniques using readily available equipment and reagents. Members were asked to inform the Secretariat if they were interested in joining the *ad-hoc* group.

Assays based on Uniformity Tests A minor change to the wording of Assays based on the average of the individual results obtained in the test for Uniformity of content or Uniformity of dose had been agreed by the BP Commission. The change affected about 60 monographs, including one from this EAG (Melatonin Capsules), and the relevant texts would be amended accordingly in the BP 2018.

463 **Assay Limits for Unlicensed Medicines** ULM(17)4

It had been suggested at the last meeting that EAG ULM should develop policy guidelines relating to Assay limits for unlicensed medicines, paying particular reference to reconstituted preparations.

The issue of non-standard Assay limits had been discussed by the BP Commission during 2015 when a number of reasons why deviation from the standard ± 5% limits might be justified were confirmed. It was pointed out that the wording in some monographs reflected the need for wider limits to allow for degradation and/or the use of overages, for example oral liquids that were supplied as powders or granules due to the instability of the active ingredient in solution or suspension.

In light of the current BP policy, and the permitted reasons to deviate from ± 5%, it was agreed that there was no need to develop separate policy guidelines on Assay limits for unlicensed medicines.

464 **Use of Unlicensed Medicines Monographs** ULM(17)5

The work undertaken on Magnesium Glycerophoshate Oral Solution noted at the last meeting (minute 454 refers) had been drawn to the attention of the British Pharmacopoeia Commission. The Commission had been pleased to note the value of the published monograph in this situation.

465 **Co-proxamol Tablets** ULM(17)6

Following concerns over toxicity and (lack of) efficacy, all marketing authorisations for Co-proxamol Tablets had been cancelled, although the product could still be prescribed on a named-patient basis for those individuals who were unable to switch to a different medicine. This position was reflected in the current edition of the British National Formulary.

A member of the BP Commission had recently raised concerns over the continued inclusion of the monograph in the BP. However, there were still a significant number of prescriptions issued for Co-proxamol Tablets each year and the monograph met a number of criteria for monograph development (it is widely used, there is a particular need for the product based on therapeutic category).

Several members confirmed that the product was widely used and that they favoured retention of the monograph. Until there was no longer a need for Co-proxamol Tablets it was agreed that the monograph should continue to be included in the BP.

466 **Extemporaneous Preparations** ULM(17)7

Members were reminded that the BP Commission had strongly supported the proposed approach of moving extemporaneous preparation information to a Supplementary Chapter rather than retaining the details in individual monographs. EAG PCY had not met since this issue was last discussed and so no further progress had been made.

467 **Supplementary Chapter V: Unlicensed Medicines** ULM(17)8

The Secretariat had met with representatives from the Regulatory Advice Unit (Inspection, Enforcement & Standards Division, MHRA) to discuss proposed amendments to Supplementary Chapter V. It had been confirmed that the section 10 exemption under the Medicines Act 1968 relating to pharmacy preparation remained in place and was invoked under Regulation 4 of the Human Medicines Regulations 2012. A number of changes had been proposed to reflect the current situation and to reflect updated guidance from the Royal Pharmaceutical Society.

Members were invited to examine the revised text which was accepted subject to minor editorial changes.

IV NEW MONOGRAPHS

468 **Work Programme** ULM(17)9

The work programme had been updated to reflect changes since the last meeting and a copy was provided for information. Members were encouraged to provide information to

assist in the development of suitable monographs, to test the suitability of draft methods and to provide details of suppliers, where possible.

In order to try and increase the output of the group, it was agreed that members should examine the current work programme with a view to identifying a minimum of three items for which they could provide information that would enable development of a monograph. The Secretariat would circulate the list and an update would be presented at the next meeting.

469 **Carvedilol Oral Suspension** ULM(17)10

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

470 **Clomipramine Oral Suspension** ULM(17)11

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

471 **Naltrexone Preparations** ULM(17)12

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

472 **Parenteral Nutrition Solutions** ULM(17)13

It had previously been intended to develop a stand-alone General Monograph for Parenteral Nutrition Solutions. it was now proposed to develop a wider General Monograph on Aseptic Preparations which would encompass Parenteral Nutrition Solutions and intra-ocular preparations. The draft monograph would be included in a future publication, subject to resolution of any outstanding points.

473 **Intraocular Injections** ULM(17)14

It had previously been agreed to include some general guidance on Intraocular Injections in the BP. It was intended to initially include guidance as part of the new Supplementary Chapter on the Aseptic Preparation of Unlicensed Medicines and then to expand the proposed new General Monograph on Aseptic Preparations to include requirements for Intraocular Injections. The draft monograph and Supplementary Chapter would be included in a future publication, subject to resolution of any outstanding points.

V MONOGRAPHS IN PROGRESS

474 **Ceftazidime Injection** ULM(17)15

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

475 **Ethambutol Oral Suspension** ULM(17)16

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

476 **Lorazepam Oral Suspension** ULM(17)17

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

VI REVISION OF MONOGRAPHS

477 **Chlorhexidine Gluconate Eye Drops** ULM(17)18

Related substances Further information had been received which supported the following impurity limits: 4-chloroaniline, not more than 1%; one impurity, not more than 1.5%; any other impurity, not more than 1%; sum of total impurities, not more than 3.5%. The amount of 4-chloroaniline varied between 0.4% and 0.6% and the proposed limit ensured a viable shelf-life for the product. Members agreed that the revised limits should be included in the British Pharmacopoeia 2018.

478 **Sodium Chloride Oral Solution** ULM(17)19

Attention had been drawn to possible contamination from the container used for Sodium Chloride Oral Solution. Members were asked if they were aware of any issues with contamination of this product and whether reference to the type of container should be included in the monograph.

From the information supplied it appeared that the presence of sodium citrate in the formulation might be responsible for deterioration of the container since it was known that certain buffers, including citrate, corroded glass. Members agreed that it was not necessary to specify the type of container in the monograph, since this aspect was adequately covered by the General Notice on Containers and by Appendix XIX B: Glass Containers for Pharmaceutical Use. However, it was agreed that in view of the potential issue with one formulation reference to the absence of visible particles should be added under Characteristics.

It was understood that licensed forms of at least one strength were now available and so the responsibility for the monograph would be transferred to the relevant Expert Advisory Group.

479 **Supplementary Chapter V F: Aseptic Preparation of Unlicensed Medicines** ULM(17)20

The new Supplementary Chapter had been published in the BP 2017. A number of minor editorial points were raised by the Vice-Chair in order to clarify the intended scope of the chapter. It was agreed that the Secretariat should make the final changes and confirm these with the Chair and Vice-Chair before 28th April.

VII INTERNATIONAL

480 **Paediatric Formulary Working Party** ULM(17)21

The Summary of Decisions from the latest meeting of the Paediatric Formulary Working Party was provided for information, together with a report from the Chair of the group that had been presented to the European Pharmacopoeia Commission.

481 **Council of Europe Resolutions** ULM(17)22

CM/Res(2016)1: Quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients Members noted that the Resolution had been included on the agenda of the November 2016 Session of the European Pharmacopoeia Commission for information. Although Resolutions were not mandatory, EU Member States were encouraged to comply. The content of the Resolution reflected UK practices and so no difficulties were expected.

VIII ANY OTHER BUSINESS

482 **Date of next meeting**

To be arranged.