BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group: Medicinal Chemicals 3

SUMMARY MINUTES

A meeting of this Expert Advisory Group was held at 151 Buckingham Palace Road, London SW1W 9SZ on Tuesday 7th October 2014.

Present: Mr V Fenton-May (*Chairman*), Professor E Williamson (*Vice-chairman*), Professor M Almond, Mr S Arkle, Mr C T Goddard, Mr P Hampshire, Dr K Pugh, Dr B Rackstraw, Dr R Torano, Mr M Tubby, Mr I R Williams.

In attendance: Mr A Evans, Ms H Corns, Mr N Vadukul, Mr J Elliott, Ms H Bowden.

Apologies: None.

INTRODUCTORY REMARKS

The Chairman welcomed Ms Hannah Bowden attending as an observer to the meeting, Mr Nash Vadukul and Mr Jack Elliott attending on behalf of the BP Laboratory.

The Chairman reminded members that Mr Wayne Jeffries should be contacted if members experienced any difficulties with their travel bookings or expenses claims.

The Chairman reiterated to members the confidential nature of the papers presented at EAG meetings and that members should declare any interests at the start of each agenda item.

I MINUTES

The minutes of the meeting held on 25th February 2014 were confirmed.

II MATTERS ARISING FROM THE MINUTES

395 The following matters arising from the meeting held on 25th February 2014 were noted.

Monographs for Omission The list EAG MC3 monographs that had been identified for potential omission from the BP had been provided to EAG ULM. Any monographs that did not fall under ULM criteria will be recommended for omission at a future BPC meeting.

ICH Guidance vs Method Capability The BPC discussed the concentration of the disregard limit at the September 2014 meeting. The BPC recommended a flexible approach be adopted.

Dissolution Requirements The Secretariat informed members that other dissolution related issues had been raised through the EAGs. The Secretariat planned to review all dissolution related matters internally before raising the items for discussion at a future BPC meeting.

Multi-dose Container Assay The Secretariat informed members that the issue regarding Assay sample preparation from multi-dose containers would be discussed within the Secretariat.

Packed Column Replacement The BP Laboratory gave an overview of work undertaken to substitute capillary GC columns for packed GC columns in BPCRS testing methods.

Outdated Monographs Outdated monographs were included within the overall work programme review and prioritisation project being undertaken by the Secretariat.

III REPORTS AND CORRESPONDENCE

396 Members' details **MC3(14)23**

Members were asked to check the circulated contact details and to inform the Secretariat of any amendments required.

397 British Pharmacopoeia Chemical Reference Substances **MC3(14)24**

The British Pharmacopoeia Chemical Reference Substances approved since the last meeting of the EAG were noted.

398 Emergency Procedures **MC3(14)25**

A copy of the 151 Buckingham Palace Road Evacuation Procedures was provided to members for information.

399 EAG Work Programme **MC3(14)26**

A copy of the work programme for EAG: MC3 was provided to members for information. Members were asked to contribute data should they have an interest in any of the products.

400 BP Updates **MC3(14)27**

The Secretariat provided members with an update on changes within the MHRA and the BP.

401 Anti-epileptic Drugs **MC3(14)28**

Members were informed that BPC had agreed that for category 1 AEDs, where CHM advised the maintenance of the patient on a specific product; an opening statement of "*'API Formulation'* from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable" should be included in BP monographs. This applied to Phenobarbital Elixir, Phenobarbital Tablets and Phenobarbital Sodium Tablets which were the responsibility of EAG MC3.

For category 2 AEDs, where CHM advised a clinical judgement was required as to whether a patient could change between different manufacturer's products; BPC agreed that an opening statement of "*'API Formulation'* from different manufacturers, whilst complying with the requirements of the monograph, may not be interchangeable" should be included in BP monographs. This applied to Clobazam Tablets and Clonazepam Tablets which were the responsibility of EAG MC3.

IV NEW MONOGRAPHS

402 Alfacalcidol Capsules **MC3(14)29**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

403 Alfacalcidol Injection **MC3(14)30**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

404 Alfacalcidol Oral Drops **MC3(14)31**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

405 **Amitriptyline Preparations:** **MC3(14)32**
Amitriptyline Oral Solution
Amitriptyline Tablets

The draft monograph for Amitriptyline Oral Solution would be included in a future BP publication, subject to comments from manufacturers.

Upon review, the Secretariat had identified the Amitriptyline Tablets monograph would benefit from an update. Members agreed that revision of the Amitriptyline Tablets monograph should be investigated and may be included in a future BP publication, subject to comments from manufacturers.

406 **Diamorphine Tablets** **MC3(14)33**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

407 **Dihydrocodeine Preparations:** **MC3(14)34**
Dihydrocodeine Injection
Dihydrocodeine Oral Solution
Dihydrocodeine Tablets
Prolonged-release Dihydrocodeine Tablets

The draft monograph for Prolonged-release Dihydrocodeine Tablets would be included in a future BP publication, subject to comments from manufacturers.

Upon review, the Secretariat had identified the Dihydrocodeine Injection, Dihydrocodeine Oral Solution and Dihydrocodeine Tablets monographs would benefit from an update. Members agreed that revision of the Dihydrocodeine monographs should be investigated and may be included in a future BP publication, subject to comments from manufacturers.

408 **Gestodene and Ethinylestradiol Tablets** **MC3(14)35**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

409 **Soluble Prednisolone Tablets** **MC3(14)36**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

V MONOGRAPHS IN PROGRESS

410 **Acarbose Tablets** **MC3(14)37**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

411 **Estradiol Vaginal Tablets** **MC3(14)38**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

412 **Fluticasone and Salmeterol Inhalation Powder, pre-dispensed** **MC3(14)39**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

413 Fluticasone and Salmeterol Pressurised Inhalation **MC3(14)40**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

414 Olanzapine Preparations: **MC3(14)41**
Olanzapine Tablets **LR 5605**
Orodispersible Olanzapine Tablets

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

415 Vecuronium Bromide Injection **MC3(14)42**

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

VI REVISION OF MONOGRAPHS

416 Preparations Containing Chloroform: **MC3(14)43**
Liquid Paraffin Oral Emulsion
Liquid Paraffin and Magnesium Hydroxide Oral Emulsion
Kaolin and Morphine Mixture

The Secretariat informed members the monographs containing chloroform as an excipient had been revised, as agreed by BPC and would be included in a future BP publication.

417 Codeine Phosphate Oral Solution Preparations: **MC3(14)44**
Codeine Linctus
Paediatric Codeine Linctus
Codeine Phosphate Oral Solution

The Secretariat informed members the monographs containing chloroform as an excipient had been revised, as agreed by BPC. In the course of the revision process, the Secretariat identified that the Codeine Linctus, Paediatric Codeine Linctus and Codeine Phosphate Oral Solution monographs could be combined into a single open strength Codeine Phosphate Oral Solution monograph. The revised combined monograph would be included in a future BP publication, subject to comments from stakeholders.

418 Cyproterone Tablets **MC3(14)45**

A manufacturer had contacted the Secretariat with a request to increase the particle size of the column used in the Assay procedure from 3.0µm to 3.5µm or to include an alternative Assay method. Members noted that there was no concern over manufacturers using alternative methods to the BP, provided equivalence was demonstrated and the methods were validated. Members agreed that the consideration would be given to increasing the particle size with the existing procedure if the manufacturer could demonstrate comparable method performance. However as no issues had been reported with the existing method, it was accepted that it would be difficult to justify allocating laboratory resources to investigate the alternative procedure.

419 Dexamethasone Sodium Phosphate Injection **MC3(14)46**

The Ph. Int. had provided a laboratory report to the Secretariat which assessed a Related substances test for the control of impurities in Dexamethasone Sodium Phosphate Injection products. The Secretariat had revised the monograph for Dexamethasone Sodium Phosphate Injection in light of the report findings. Members agreed that the revised method was suitable for inclusion in the BP monograph.

Whilst revising the Related substances test, the Secretariat had noted that there appeared to be an inconsistency between the expression of strength of the products on the UK market and the labelling statement in the BP monograph 'The content of active ingredient is stated as the amount of dexamethasone phosphate in a suitable dose-volume'. It was noted that he EMA had ruled that the strength of these products should be expressed in terms of dexamethasone (base). Members agreed that the monograph should be revised to express the strength in terms of dexamethasone, in-line with the EMA decision.

The revised monograph would be included in a future BP publication, subject to comments from stakeholders.

420 **Diazepam Preparations:** **MC3(14)47**
Diazepam Injection
Diazepam Oral Solution
Diazepam Rectal Solution
Diazepam Tablets

Upon review, the Secretariat had identified all Diazepam preparation monographs would benefit from an update. Members agreed that revision of the Diazepam product monographs should be investigated and may be included in a future BP publication, subject to comments from manufacturers.

421 **Ergocalciferol Injection** **MC3(14)48**

The Secretariat had received a request to remove the fixed strength requirement from the Ergocalciferol Injection monograph and amend the characteristics to recognise that the product could appear as a colourless liquid. Members agreed to the proposed revision and also identified that the Ergocalciferol Injection monographs would benefit from an update.

The revised monographs may be included in a future BP publication, subject to comments from manufacturers.

422 **Ethinylestradiol Tablets** **MC3(14)49**

The Secretariat had received a request to revise the Uniformity of content test as the published monograph was product strength specific. Members agreed to the proposed revision and to investigate a Related substances test for this monograph.

The revised monograph may be included in a future BP publication, subject to comments from manufacturers.

423 **Hydroxyzine Oral Solution** **MC3(14)50**

The Secretariat had received additional information regarding adducts formed due to interaction between hydroxyzine and fructose. The revised monograph may be included in a future BP publication, subject to comments from manufacturers.

424 **Levonorgestrel Tablets** **MC3(14)51**

The Secretariat provided members with a tabled paper and asked for comments to be submitted by correspondence.

VII EUROPEAN PHARMACOPOEIA COMMISSION

Members were directed to log-in to the BP website to view the latest text from the Ph. Eur.

VIII ANY OTHER BUSINESS

No further items were raised for discussion.

Date of Next Meeting
Wednesday 25th February 2015.