BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC2: Medicinal Chemicals

SUMMARY MINUTES

A meeting of this Expert Advisory Group (EAG): Medicinal Chemicals 2 (MC2) was held via videoconference on the 10th and 13th May 2022.

Present: Dr G Cook (*Chairman)*, Mr C Goddard (*Vice-Chairman*), Prof J Birchall, Ms K Boon, Mr J Cowie, Mr E Hook (10th May session only), Prof J Miller, Dr A Ruggiero and Mr N Wynne.

In attendance: Ms H Corns, Ms A Thomson, Mr C Thompson, Mr S Greatorex, Ms M Guler and Ms F Norris.

Apologies: Dr K Foster and Mr E Hook (13th May session only).

530 Introductory Remarks

Welcome The Chairman welcomed members to the meeting, Mr C Thompson and Mr S Greatorex from the BP Laboratory, and Ms M Guler and Ms F Norris from the Agency's Governance division.

Confidentiality Members were reminded that all papers and minutes were confidential and should not be disclosed outside the BP Commission.

Declaration of Interests Members were reminded that they are required to inform the Secretariat of any changes to their interests throughout the year.

531 BP Update **MC2(22)01**

Members were provided with an update on recent BP activities and personnel changes.

532 MINUTES

The Minutes and Summary Minutes from the meeting held on the 3rd and 4th November 2021 were confirmed without amendment.

533 MATTERS ARISING FROM THE MINUTES **MC2(22)02**

Matters arising and correspondence items from the meeting held on the 3rd and 4th November 2021 were noted. Members had no additional comments.

MONOGRAPHS

Dr G Cook, Mr J Cowie and Mr E Hook declared interests in one or more agenda items and appropriate action was taken.

534 Clopidogrel Tablet preparations: **MC2(22)03**
Clopidogrel Hydrogen Sulfate Tablets (New)
Clopidogrel Besilate Tablets (New)

Clopidogrel Hydrochloride Tablets (New)

The draft new monographs would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

535 Imatinib preparations: MC2(22)04
Imatinib Tablets (New)
Imatinib Capsules (New)
Imatinib Oral Solution (New)

The draft new monographs would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

536 Donepezil preparations: MC2(22)05
Donepezil Oral Solution (New)
Donepezil Orodispersible Tablets (New)
Donepezil Tablets (New)

The draft new monographs would be included in a future BP publication, subject to amendments and comments from manufacturers.

537 Dapsone Tablets (Revised) MC2(22)06

Related substances Members endorsed replacement of the TLC method with the gradient LC method in the Dapsone drug substance monograph (Ph. Eur. Supplement 10.6) which was found to be suitable by the BP Lab.

Limits of NMT 0.4% each for impurities A and B, 0.3% for impurity C, 0.2% for any individual unspecified peak and 2.0% for total impurities were accepted, subject to public consultation.

Assay Members endorsed inclusion of the donor manufacturers' assay isocratic HPLC method. All tablet samples tested passed the content requirement of 95.0 to 105.0%.

538 Chlorhexidine preparations: MC2(22)07
Chlorhexidine Gluconate Dental Gel (Revised)
Chlorhexidine Acetate Irrigation Solution (Revised)
Chlorhexidine Mouthwash (Revised)

Chlorhexidine Gluconate Dental Gel - Identification Members recommended that the separate light absorption and Assay peak comparison tests were replaced with a LC/UV-DAD procedure which was agreed, subject to stakeholder comments.

Chlorhexidine Gluconate Dental Gel – Acidity or alkalinity The Secretariat agreed to investigate whether the acidity or alkalinity test needed to be retained in the monograph.

Chlorhexidine Gluconate Dental Gel - Related substances The BP Lab found that the related substances test was suitable and recommended the use of a ReproSil-Pur Basic C18 column, as the resolution requirement was not met using the Wakosil II 5C18 RS column. Members accepted the laboratory report recommendations, and noted that as impurity P and impurity N under-responded when compared to chlorhexidine, signal to noise system suitability requirements were needed for solutions 3 and 6 (80 and 20 respectively).

Chlorhexidine Irrigation Solution - Title Members endorsed the recommendation to change the monograph title to Chlorhexidine Acetate Irrigation Solution, as a product had been licensed that contained Chlorhexidine Gluconate Solution and this did not fall within the definition of the monograph.

Chlorhexidine Irrigation Solution - Content Members questioned whether the content limit of 95.0 to 105.0% may be too restrictive in light of the revised related substances limits. The Secretariat agreed to investigate further and to seek stakeholder advice.

Chlorhexidine Irrigation Solution - Identification The laboratory report confirmed that a LC/UV-DAD identification test was suitable for inclusion in the monograph. Members agreed that the revised test should be adopted.

Chlorhexidine Irrigation Solution – Related substances Members accepted the laboratory assessment which confirmed that the revised related substances test was suitable for the monograph.

The laboratory reported a correction factor of 2.7 for impurity N.

Members agreed the recommendation to increase the limit of NMT 1.0% for impurity N to 2.7% to accommodate the correction factor identified by the lab, and the total impurity limit was increased from 3.0% to 4.5%. As the limit for impurity N was a significant contributor to the total impurities, members concurred that excluding impurity N from the impurity total would offer more effective control of impurities. A total impurity limit of 2.0%, excluding impurity N, was agreed subject to stakeholder comments.

Chlorhexidine Irrigation Solution - Assay Members accepted the laboratory recommendation that the revised Assay, harmonised with the related substances test, was found to be suitable for the monograph with reduced solution concentrations which improved peak shape.

Chlorhexidine Mouthwash - Content Members questioned whether the content limit of 95.0 to 105.0% may be too restrictive in light of the revised related substances limits. The Secretariat agreed to investigate further and to seek stakeholder advice.

Chlorhexidine Mouthwash - Identification The laboratory report confirmed that a LC/UV-DAD identification test was suitable for inclusion in the monograph. Members agreed that the revised test should be adopted.

Chlorhexidine Mouthwash – Related substances The gradient LC related substances method submitted by an MAH was found to be suitable by the BP laboratory.

Members agreed that the expression of total impurities recommendation for Chlorhexidine Acetate Irrigation Solution, also applied to the Chlorhexidine Mouthwash monograph, as a limit of NMT 3.5% had been included for impurity N. A total impurity limit of 2.0%, excluding impurity N, was agreed subject to stakeholder comments.

Chlorhexidine Mouthwash – Assay Members accepted the laboratory recommendation that the revised Assay, harmonised with the related substances test, was found to be suitable for the monograph with reduced solution concentrations which improved peak shape. The laboratory recommended that a peak symmetry requirement of 0.8 to 2.0 was adopted which the Secretariat agreed to include in the revised monograph.

539 Fenofibrate preparations: MC2(22)08

Fenofibrate Capsules (New)

Fenofibrate Tablets (New)

The draft new monographs would be included in a future BP publication, subject to amendments and comments from manufacturers.

540 Bupivacaine Injection preparations: MC2(22)09

Bupivacaine Heavy Injection (Revised)
Bupivacaine Injection (Revised)

Introductory note EAG PCN had advised that an introductory note was included in both texts to exclude the monographs from being applied to liposomal formulations of bupivacaine injection preparations. Members accepted the recommendation.

Impurity F (2,6-dimethylaniline) limits The draft revised monographs that were made available for stakeholder comments had included a limit of NMT 10 ppm for impurity F. Comments had been received requesting that the limit for impurity F was increased to NMT 200 ppm. Results had been provided, demonstrating impurity Fat levels above 10 ppm and that the application of ICH M7(R1) gave a 0.03% (300 ppm) limit for this impurity.

Members accepted that a higher limit of impurity F was required, however, also agreed that the data provided was limited. Members requested that additional information was sought including the maximum daily dose on which the calculation had been based.

FOR INFORMATION

541 Out of Stock BPCRS **MC2(22)10**

The Secretariat reviewed the out-of-stock BPCRS for monographs relevant to EAG MC2 and presented these to the group.

542 CST Changes **MC2(22)11**

Members were provided with a summary of changes to Ph Eur general chapter 2.2.46 following the completion of a harmonised text for Chromatographic Separation Techniques, delivered through the PDG framework.

543 MC2 Work status and updates **MC2(22)12**

The MC2 Work Programme was presented to members for information.

544 Ph. Eur. Updates **MC2(22)13**

The Secretariat thanked members for their contributions to the Pharmeuropa 34.1 review and confirmed that none of the texts in the Pharmeuropa 34.2 review had been assigned to MC2.

545 ANY OTHER BUSINESS

None.

546 NEXT MEETING

The next meeting would be held on Wednesday 9th November 2022, and if held virtually, a second session on Thursday 10th.