BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC1: Medicinal Chemicals

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 1 (MC1) was held at 151 Buckingham Palace Road, London SW1W 9SZ on Friday 15 June 2018.

Present: Professor A G Davidson *(Chairman),* Professor D Cairns, Mr D Deutsch, Mr P Fleming, Dr E Gray, Dr J Lough and Mr D Malpas.

In attendance: Ms H Corns, Dr K Radi, Ms G Li-Ship, Ms K Busuttil and Ms M Nanasi.

Apologies: Dr J C Berridge, Dr E Bush, Mr A J Caws

516 **Welcome** The Chairman welcomed Ms G Li-Ship, who attended the meeting as an observer; and Ms M Nanasi and Ms K Busuttil from the BP Lab.

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

Declaration of Interests Prof D Cairns and Mr D Malpas declared interests in one or more agenda items and appropriate action was taken.

517 **Emergency evacuation procedure**

The emergency evacuation procedure for Buckingham Palace Road was noted.

518 **BP Update**

Members were provided with an update on EAG's membership renewal process, on BP staff changes and on the Agency's accommodation move.

519 **MINUTES**

The minutes and summary minutes of the meeting held on 5 December 2017 were confirmed.

520 **Matters Arising**

Matters arising from the 5 December 2017 meeting were noted.

521 **Celecoxib Capsules (new)**

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

522 Ritonavir preparations (new):
Ritonavir Oral Solution
Ritonavir Tablets

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

523 Leflunomide Tablets (new)

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

524 Phenytoin preparations (revision):
Phenytoin Capsules
Phenytoin Injection
Phenytoin Oral Suspension
Phenytoin Tablets

Production (Capsules & Tablets only) A production statement would be included for the control of dissolution until suitable test procedures were identified.

Dissolution (Capsules, Oral Suspension & Tablets only) Potential dissolution test procedures had been identified and laboratory assessment prior to publication was agreed. Members confirmed that should further procedures be provided by manufacturers, that these should be included within the testing protocol.

Monograph consultation Members confirmed the decision to take forward previously agreed revised tests ahead of the revisions to remove chloroform and the outcomes of the dissolution test assessments, which required further lab work to be carried out. Draft revised monographs with the first phase of revisions would be posted for consultation prior to the next EAG meeting.

525 Paracetamol preparations (revision)

Combination product monographs It was agreed that methods should be investigated to revise monographs as follows:
Paracetamol and Caffeine Tablets – replace Identification test B
Soluble Paracetamol and Caffeine Tablets – replace Identification test C
Co-codamol Tablets – revise Related substances test
Effervescent Co-codamol Tablets – include an identification test for paracetamol, revise Related substances test
Co-codamol Capsules – revise Related substances test
Co-dydramol Tablets – revise Related substances test
Paracetamol, Codeine Phosphate and Caffeine Tablets – replace Identification test D, revise Related substances test
Paracetamol, Codeine Phosphate and Caffeine Capsules – replace Identification test D, revise Related substances test

Paracetamol-only product monographs It was agreed that methods should be investigated to revise monographs as follows:
Paracetamol Tablets – review need for Identification tests B and C, revise Assay
Dispersible Paracetamol Tablets – revise Assay
Effervescent Paracetamol Tablets – revise Assay

Soluble Paracetamol Tablets – revise Assay
Paracetamol Capsules – consider harmonising Dissolution with Assay
Paediatric Paracetamol Oral Solution – revise Related substances
Paracetamol Oral Suspension - revise Related substances
Paracetamol Suppositories – replace Identification test B, revise Assay

The highest priority were the replacement of TLC Related substances tests in the combination products and manufacturers would be contacted to support the revision of these monographs.

526 Pyrimethamine Tablets (revision)

Dissolution A dissolution requirement of not less than 75% (Q) in 45 minutes would be drafted in the monograph and posted on the BP website for consultation.

Related substances A secondary peak limit of not more than 0.2% aligned with ICH guidance was agreed and would be drafted in the monograph and posted on the BP website for consultation.

527 Mebendazole preparations (new)
Mebendazole Chewable Tablets
Mebendazole Oral Suspension

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

528 Abacavir and Lamivudine Tablets (revision)

Lamivudine impurity J An increase from 0.2% to 0.5% for impurity J was agreed by members subject to confirmation that this specification had been accepted by TGA.

529 Propofol Injection (revision)

Identification B Members agreed to delete Identification test B as the infrared absorption spectrum was sufficient for confirmation of identity.

Globule Size It had been highlighted that the methods suggested as alternatives were not interchangeable, and that the same limit was not appropriate for all analytical techniques. As no universal test description and limit was found acceptable, members agreed to delete the test and to include a production statement to assure the necessary control of Globule size.

530 Chloroquine Sulfate Tablets (revision)

Assay It would clarified in the Chloroquine Sulfate Tablets monograph that the titration was taken to the first inflection point to explain the difference in the amounts of chloroquine sulfate were defined as equivalent to the same amount of 0.1M perchloric acid in the drug substance and tablets monographs.

It was noted that an amount of 20.9 mg corresponds to the non-hydrous product compound $C_{18}H_{26}ClN_3$, H_2SO_4 and the monograph content refers to $C_{18}H_{26}ClN_3$, H_2SO_4, H_2O. The amount would be amended to 21.8 mg to allow users to determine content equivalent to the hydrated compound stated in the content requirement.

531 MC1 Work status and updates

The MC1 work programme was presented to members for information.

532 Pharmeuropa Update

An update on changes to Ph. Eur. monographs that affected MC1 monographs was presented to members.

533 AOB

No items were raised.

534 Date of next meeting

Wednesday 5 December 2018