BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC3: Medicinal Chemicals 3

SUMMARY MINUTES

A meeting of this Expert Advisory Group (EAG): Medicinal Chemicals 3 (MC3) was held in hybrid format (in-person and via MS Teams) on Wednesday 26th March 2025.

Present in person: Mr I Williams (Temporary Chair), Mr C Giartosio (Co Vice-Chair), Mr C Goddard (Co Vice-Chair), Mr M Coxon, Mr P Hampshire and Mr C Turville.

Present via MS Temas: Dr V Ibekwe, Dr LM Lane, Mr J Mehta, Prof Y Perrie (*absent for item discussed under minutes 692)*.

In attendance in person: Dr C Swann, Dr M Dmitriieva, Dr B Bahsoun, and Mr S Greatorex (BP Lab).

Observers: Mr S Hoare, Mr M Whaley and Ms S Elliott.

Apologies: Ms K Foster, Ms D Obaid and Dr Ron Torano.

I General Matters

678 Introductory Remarks

Welcome The Chair welcomed members to the MC3 meeting and extended a special welcome to Professor Perrie, a BP Commission member and a newly appointed expert on MC3. He also welcomed Mr Hoare, Mr Whaley, and Ms Elliott, who were attending as observers.

Conflict of interest Members were reminded that they were required to declare any relevant interests at the start of agenda items.

Expense claims Members were informed that expense claims, and any queries about expenses, should be emailed to the Committee Services Team at the MHRA.

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

679 MHRA and BP updates MC3(25)01

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

II Minutes

680 Minutes MC3(25)02

The Minutes from the meeting held on 29th February 2024 were confirmed without amendment.

681 Summary Minutes **MC3(25)03**

The Summary Minutes from the meeting held on 29th February 2024 were confirmed without amendment.

III Matters Arising

682 Matters Arising from the Minutes **MC3(25)04**

The following matters arising and correspondence items from the meeting held on the 29th February 2024 were noted.

IV Discussion Topics

683 BP Sustainability update **MC3(24)05**

Members received an update on the BP's sustainability initiatives, including scaled-down methods to reduce environmental impact. Draft monographs would be assessed for sustainability, and a standing sustainability item would be added to the agenda for future meetings.

V Monographs for BP 2027

Mr Hampshire declared interests in one or more agenda items and appropriate action was taken.

684 Ropinirole preparations **MC2(25)06**
Ropinirole Tablets (New) **Annexes 1-5**
Ropinirole Prolonged Release Tablets (New)

The Secretariat presented the challenges with the assay sensitivity and prolonged dissolution times and poor recovery were discussed with members. The laboratory would continue to investigate method improvements including alternative solvents and use of homogenisers.

VI New Monographs

Mr Hampshire declared interests in one or more agenda items and appropriate action was taken.

685 Atracurium Besilate Injection (New) **MC3(25)07 Annex 1-7**

Title Members agreed to change the title to include "*infusion*" as well as "*injection*", as the product could be administered by either route.

Definition Members discussed specifying the isomer ratio for Atracurium Besilate. Members agreed to retain the current wording noting the presence of three isomers, with the option to revisit pending MAH feedback.

Content Members agreed upon the proposal of the content limit at 90-115% in line with the USP.

Identification Members approved the drafted HPLC-UV procedure derived from the assay method, with a proposal for the BP laboratory to further investigate whether the UV spectrum, in conjunction with retention time, provided sufficient specificity for active pharmaceutical ingredient (API) identification. The identification wording was revised to reflect that Atracurium Besilate comprises three isomers, all visible in the chromatogram.

Related substances Members agreed with the proposed limits for impurities with impurities over 0.2% identified using the European Pharmacopoeia impurity peak identification standard.

Assay Members approved the proposal of the assay procedure based on an HPLC method with UV detection, consistent with the European Pharmacopoeia and aligned with the draft USP monograph for the injection form of Atracurium Besilate.

Labelling Members agreed with the product labelled in terms of Atracurium Besilate, stored at 2-8°C in a refrigerator, with an 18-month shelf life.

Standards The method would require the establishment of an Atracurium Besilate BPCRS and, an Atracurium for peak identification BPCRS and Atracurium for impurity F identification BPCRS. Currently, EPCRS would be used for peak identification.

Method Evaluation Assessment The method evaluation concluded that the presence of multiple isomers and relatively high impurity levels posed a potential risk to method sensitivity.

686 Naloxone Nasal Spray (New) **MC3(25)08 Annexes 1-5**

Definition Members agreed that the product should be described as "*naloxone hydrochloride*" rather than just "*naloxone*" to ensure consistency with the injection monograph.

Content The agreed limits of 95-105% were confirmed.

Identification Members confirmed the proposal of an HPLC-UV diode array identification test and to compare the entire spectra rather than specifying exact wavelengths for the maxima and minima.

Acidity Members agreed to remove the pH test from the monograph.

Related substances Members had agreed to an unspecified impurity limit of 0.5%. As none of the listed impurity limits had exceeded this threshold, individual control of named impurities had not been considered necessary. The laboratory was to determine whether a resolution-based system suitability requirement should be included.

687 Hydrocortisone Tablets (New) **MC3(25)9 Annexes 1-7**

Content Members agreed to the standard content limits of 95-105%.

Identification Members agreed on the proposed IR test based on the USP monograph.

Dissolution A requirement of 75% in 30 minutes was agreed by members with editorial correction to the draft monograph including incorrect dissolution time sample and concentration calculations to be adjusted on the lowest product strength.

Related Substances Members agreed to the drafted related substances test, with the intention of exploring a scaled method approach to support stability assessments.

Assay Members agreed with the proposed method.

Standards The BPCRS and EPCRS standards available were deemed sufficient for this monograph

Method Evaluation Assessment The method evaluation concluded that laboratory assessment was advisable prior to publication.

VII Major Revisions

Mr Hampshire declared interests in one or more agenda items and appropriate action was taken.

688 Diazepam Preparations (Revision) **MC3(25)9 Annexes 1-7**
Diazepam Tablets
Diazepam Injection
Diazepam Oral Solution

Diazepam Rectal Solution

Identification An HPLC-UV/diode array method using the assay procedure was agreed by members.

Acidity Members agreed to remove the pH test from the formulations except for the rectal solution, where it might be more critical.

Dissolution Members agreed the inclusion of specific signal-to-noise ratios , and ensure consistent application of system suitability tests across the family of monographs and using a weight per mL measurement due to some formulation containing propylene glycol (Diazepam Injection).

Related substances Members agreed on the assay method was based on the related substances procedure and verified in the laboratory during testing.

689 Oxazepam Tablets **MC3(25)11**
Annexes 1-6

Content Members agreed to change the content limits from 90-110% to the standard 95-105%.

Identification Members agreed to retain the current IR method using chloroform, with the lab exploring alternative solvents. HPLC was noted as a potential alternative.

Dissolution Members discussed using a standard solution for dissolution testing, specifying ambient temperature (15–25°C), ensuring appropriate S/N ratios, and agreed to include light protection using amber glassware.

Related Substances The TLC method was replaced with an HPLC method aligned with the Ph. Eur. API monograph, including impurities A–E, a 0.2% limit for unspecified impurities, and a 1% total limit. A resolution requirement of 1.5 between oxazepam and peaks A/E was added.

Assay The same HPLC gradient method would be used, with the lab to assess feasibility of an isocratic alternative.

BPCRS Standards A new BPCRS standard would be established for use in the HPLC procedures.

690 Naloxone Injection **MC3(25)12**
Annexes 1-4

Identification Members agreed to replace the TLC method with HPLC-UV/DAD with IR considered unsuitable. The assay method was supported for identification, subject to lab verification.
Labelling Members approved the change to update a critical dosing error (20 mg/mL for neonatal use) immediately, with a letter of amendment requested for BP 2026.

VIII Issues reported by users

Mr Coxon declared interests in one or more agenda items and appropriate action was taken.

691 Morphine Tablets (Revision) MC3(25)13 Annexes 1-4

The Secretariat presented ongoing MAH concerns with meeting the resolution requirement between impurity F and morphine sulphate in the BP method. Members agreed to revise the SST to a peak-to-valley ratio of ≥2.0, aligning with the Ph. Eur. Mr Goddard raised the wide assay limits (±7.5%), to be reviewed in a future update.

692 Clobetasol Scalp Application (Revision) MC3(25)14 Annexes 1-5

The Secretariat outlined concerns raised by multiple MAHs regarding the Clobetasol Scalp Application monograph (BP 2015), highlighting three main issues: the system suitability requirement had become unachievable due to changes in the EP Clobetasol CRS, which no longer contained impurity C; Solution 3 in the assay had been redundant; and impurity F lacked a standard for control. The original intent had been to measure resolution between the API and impurity J, but this was later changed to impurity C without clear documentation. Members approved the proposed revisions, which reinstated resolution between the API and impurity J, removed Solution 3, and deleted the instruction to identify impurity F using EPCRS.

693 Estradiol Vaginal Tablets (Revision) MC3(25)15 Annexes 1-3

Members approved updating the mobile phase composition in BP 2026 where the gradient was incorrectly specified.

IX For Information

694 European Pharmacopoeia **MC3(25)16**

The Secretariat provided an update on the European Pharmacopoeia and thanked members for their support of the Pharmeuropa 37.1.

X

695 MC3 work programme **MC3(25)17**

The MC3 Work Programme was presented to members for informational purposes.

XI

696 BPCRS update **MC3(25)18**

The Secretariat presented an update on one out of stock BPCRS with two additional BPCRS used in Isosorbide preparations were no longer available due to shipping restrictions, as they had been classified as explosive. These were to be replaced with European Pharmacopoeia CRSs (EPCRS).

XII Any Other Business

697 The Secretariat collected the names of members who had opted not to claim fees for the meeting.

XIII Next meeting

698 Members were informed that the next meeting would be a virtual meeting held in September 2025.