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 at 10 South Colonnade, London E14 4PU on Tuesday 13 May 2025.

Present: Dr G Cook *(Chair)*, Mr C Goddard (*Vice-Chair*), Mr J Rickard (*Vice-Chair)*, Mr M Ali, Dr K Boon, Dr K Chan, Dr S Ho, Mr E Hook, Prof J Miller, Dr A Ruggiero and Dr Z Smith.

In attendance: Ms H Corns, Ms A Thomson, Mr R Legg, Ms R Feltham, Mr S Hoare, Dr M Dmitriieva (MC2(25)01 only), Mr R Smith (MC2(25)05 only), Dr S Greatorex (BP Lab) and Ms J Portner (BP Lab).

Apologies: Prof J Birchall, Mr J Cowie, Dr K Foster and Mr C Natarajan.

642 Introductory Remarks

Welcome The Chair welcomed Mr S Hoare, Head of Standards & Regulatory Governance, as an observer, and Dr M Dmitriieva and Mr R Smith from the BP Secretariat. Dr S Greatorex and Ms J Portner were welcomed 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 Members were reminded that they are required to inform the BP Secretariat of any changes to their interests throughout the year via email to Agency's Committee Services Team.

643 BP Update **MC2(25)01**

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

644 MINUTES

The Minutes and Summary Minutes from the meeting held on 12 and 14 November 2024 were confirmed without amendment.

645 MATTERS ARISING FROM THE MINUTES **MC2(25)02**

Matters arising and correspondence items the meeting held on 12 and 14 November 2024 were confirmed.

MONOGRAPHS

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

646 Co-careldopa preparations (Revised): MC2(25)03
Co-careldopa Prolonged-release Tablets
Co-careldopa Tablets

Production Members endorsed the inclusion of a production statement to control hydrazine, in the absence of a suitable test.

Identification The BP Laboratory assessment demonstrated the suitability of HPLC-UV/DAD for identification of both drug substances. Members accepted the laboratory findings and confirmed the inclusion of the test in the monographs.

Hydrazine In the absence of a suitable test to include in the monograph for the control of hydrazine which is been identified as a genotoxic impurity of carbidopa, control through a production statement had been put forward and accepted by members.

Related substances The related substances method, a single chromatographic procedure for impurities of both drug substances, was found to be suitable by the BP Lab. Further laboratory work will be performed to investigate Carbidopa impurity 2.

Related substances limits (Tablets only) Members endorsed revision to the limits in the monograph for impurities A, B, and C; as well as revision to the reporting thresholds and total impurity limit.

Related substances limits (Prolonged-release Tablets only) Members endorsed revision to the limits in the monograph for impurities A, B, and C; as well as revision to the reporting thresholds and total impurity limit.

Assay The BP Lab had found the Assay method, harmonised with the related substances conditions, to be suitable for the monographs, which was accepted by members. All samples tested were able to meet the drafted content limits.

647 Paclitaxel preparations (New): MC2(25)04
Paclitaxel Sterile Concentrate
Paclitaxel for Infusion

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

648 Erlotinib Tablets (New) MC2(25)05

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

649 Prochlorperazine preparations (Revised): MC2(25)06
Prochlorperazine Tablets
Prochlorperazine Buccal Tablets
Prochlorperazine Injection

Title (Buccal Tablets) Members questioned whether the monograph title should be 'Oromucosal Tablets' rather than 'Buccal Tablets', which the Secretariat agreed to raise with EAG:PCN.

Protection from light statement (all monographs) Due to the rapid degradation of prochlorperazine under white light, the inclusion of an appropriate statement was endorsed by members.

Colour / Clarity of solution (Injection) Members raised a concern regarding the absence of a test for colour of solution, as the SmPC for one manufacturer stated to not use discoloured solutions. The Secretariat agreed to investigate the need for a colour test in the draft monograph.

Identification (Injection) Members agreed that a test for the Mesilate counter-ion test should be included, as two salt forms were present across the monograph family. The BP Laboratory will investigate whether methanesulfonic acid can be detected in either the Related Substances or Assay tests, and included into the monograph as a UV/DAD test.

Acidity (Injection) Assessors advised that the acidity requirement of 5.5 – 6.5 should be retained, which members agreed.

Dissolution (Tablets, Buccal Tablets) The HPLC method, based on a manufacturer's method and confirmed to be acceptable by the BP Lab, was accepted by members subject to stakeholder comment.

Related Substances (all monographs) Members endorsed the revision of the test, that uses an equivalent and more readily available column. The test included a S/N SST requirement for solution (4) of 15 minimum due to 1.4 correction factor for impurity C.

Assay (all monographs) The drafted assay test, based on a manufacturers method and harmonised with the dissolution conditions was found suitable for inclusion in the monographs by the BP Laboratory.

650 Indapamide preparations (Revised): MC2(25)07
Indapamide Tablets
Indapamide Prolonged-release Tablets

Production (Prolonged-release Tablets only) A request to increase the impurity C limit to 1000 ppm had been submitted, members accepted the justification for aligning the limit to the maximum daily dose of the prolonged-release formulation of 1.5 mg.

Content (Tablets only) Members accepted the assessors' recommendation to revise the content expression in terms of anhydrous indapamide. It was noted that a change to the content declaration in the BP monograph would not require a change in a manufacturer's established practice, as no potentially serious risk had been identified.

Impurity A It was confirmed no specific test for Impurity A was required as it was a process impurity that would be controlled through use of a drug substance compliant with the Ph Eur Indapamide monograph.

Impurity C (Tablets only) Members confirmed that the drafted test should be retained.

Related substances Members confirmed that the revised method should be retained, due to the improved impurity separation that allowed control of an indapamide-lactose adduct. Members endorsed using a peak to valley ratio of at least 10 as the system suitability criteria.

Related substances limits (Tablets only) The Secretariat reviewed the published limits and identified that the limit for unspecified impurities was tighter than ICH Q3B expectations. A revised limit of 0.5% was agreed by members, subject to stakeholder comment.

Related substances limits (Prolonged-release Tablets only) Members confirmed that the published unspecified impurities limit of 0.5% should be retained, in-line with ICH Q3B guidelines. Members requested that impurity B, with a specified limit of 1.0%, should be excluded from the total impurities limit, which the Secretariat agreed to implement.

651 Docetaxel Sterile Concentrate (New) **MC2(25)08**

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

652 Timolol preparations: **MC2(25)09**
Timolol Tablets (Revised)
Timolol Eye Drops (Revised)
Timolol Eye Gel (New)

Timolol Eye Gel The draft new monograph for Timolol Eye Gel would be included in a future BP publication, subject to comments from manufacturers.

Content (Tablets) Members agreed to tighten the content requirement from 90.0 – 110.0% to 92.5 – 105.0%, as advised by the MHRA assessors, and with the relatively low limit for total impurities of 1.5% in mind.

Identification (Tablets) Members approved the proposal to replace the existing TLC procedure with UV/DAD and concordant retention time in the Assay. The Secretariat had removed the separate test for the maleic acid component, as only one form of the drug substance was used in UK licensed products.

Dissolution (Tablets) A new test had been drafted, utilising basket apparatus at 100 rpm, a 0.1M hydrochloric acid medium and determination of content by LC, utilising harmonised chromatographic conditions with the Related substances and Assay tests. A limit of at least 80% (Q) in 30 minutes had been included which encompassed UK approved product specifications. Members supported the adoption of the drafted test, if a simpler procedure was not identified.

Related substances (Tablets) The Secretariat had updated the monograph to include a HPLC procedure, known to control at least two of the degradation products and utilising harmonised chromatographic conditions with the Dissolution test. Proposed limits were accepted by members and laboratory work to establish a new standards was endorsed.

Assay (Tablets) The Secretariat proposed replacement of the non-specific absorbance test with the USP Timolol Maleate Tablets HPLC Assay procedure, which was accepted by members subject to public consultation.

Impurities (Tablets) A transparency statement had been included to refer to impurities B and D listed under the Timolol Maleate drug substance monograph.

Content (Eye Drops) Members agreed to tighten the content requirement from 90.0 – 110.0% to 95.0 – 105.0%. This was endorsed by the MHRA assessors.

Identification (Eye Drops) Members approved the proposal to replace tests A and B, infrared and colour change (maleate), with UV/DAD and concordant retention time in the Assay. Members supported the removal of chlorinated solvent use, with it being environmentally beneficial.

Acidity or alkalinity (Eye Drops) Members endorsed retaining a pH requirement in the monograph, with the revision to assessing on the formulated product as-is, without a specific test concentration.

Related substances (Eye Drops) The Secretariat had updated the monograph to include an isocratic elution HPLC procedure, that detects impurities B, D and G. A resolution requirement of at least 1.5 between the peaks due to impurities G and B was accepted. Proposed limits would be subject to change, following laboratory evaluation, and stakeholder consultation.

Assay (Eye Drops) The Secretariat had proposed replacement of the non-specific absorbance test with the HPLC procedure harmonised with the drafted related substances test. This was accepted by members subject to laboratory confirmation of suitability.

Storage (Eye Drops) A storage instruction statement had been included in the revised monograph in line with the product SmPCs to state the product should be protected from light.

Impurities (Eye Drops) A transparency statement had been included to refer to impurities B, D and G listed under the Timolol Maleate drug substance monograph.

653 Carbocisteine preparations (New): MC2(25)10;

Carbocisteine Capsules

Carbocisteine Oral Solution

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

654 Pyridostigmine Tablets (Revised) MC2(25)11

Content MHRA assessors advised that the upper limit could be tightened to 105% but the lower limit should remain at 92.5%. Members agreed, subject to stakeholder comment.

Identification The draft revised identification method, replacing identification tests A, B and C with a UV/DAD test utilising results from the revised Assay method was accepted by members, subject to stakeholder comment.

Dissolution A new dissolution test method had been drafted into the monograph, with a limit of 75% (Q) in 45 minutes, which was endorsed by members.

Related substances The related substances method was revised to include a reporting threshold, as well as an 'any other secondary peak' limit. BP laboratory work would be performed as part of BPCRS establishment.

Assay An assay method was drafted, based on the currently published Related substances method. Members accepted this for inclusion in the monograph, subject to stakeholder comment.

A declared content for the established Pyridostigmine Bromide BPCRS was required for use in the Assay.

655 Salbutamol preparations (Revised): MC2(25)12

Salbutamol Tablets
Salbutamol Pressurised Inhalation
(Salbutamol Injection
Salbutamol Nebuliser Solution)
Salbutamol Oral Solution

Identification B (Tablets and Injection) Members noted that the test for sulfates, as written, required that both reactions A and B for sulfates to be demonstrated. It was more common to specify reaction A for identification of sulfates. The Secretariat agreed to investigate whether both reactions were required.

Dissolution (Tablets only) Members endorsed a correction to the dissolution medium to 0.1M hydrochloric acid. Members requested that the resolution requirement was removed as a system suitability test.

Assay (Oral Solution only) Members endorsed the inclusion of a wider peak symmetry of 0.8 – 3.0 in the monograph as a system suitability requirement.

Related substances (Injection, Nebuliser Solution and Pressurised Inhalation, suspension) An amendment and adjusted retention time in the Injection and Pressurised Inhalation monograph was agreed via correspondence for the inclusion in the BP 2026. The same amendments to the Nebuliser Solution method would be made once relative retention information for additional impurities was known.

656 Flurbiprofen preparations: MC2(25)13

Flurbiprofen Sodium (Revised)
Flurbiprofen Tablets (Revised)
Flurbiprofen Eye Drops

Content (Tablets) Members proposed revising the content limits to 95%-105%, which could be accommodated by all licensed products. The Secretariat agreed to amend the draft monograph to reflect this.

Identification (Tablets) The Secretariat proposed the removal of identification tests B and C, and test A (an IR test) was sufficiently discriminatory. Members agreed with this proposal subject to stakeholder comment.

Dissolution (Tablets) A dissolution test had been drafted (based on the USP) for inclusion in the monograph with a limit of 75% (Q) in 45 minutes which accommodated UK licensed products. Members endorsed the inclusion of the test subject to stakeholder comment.

Related Substances (Tablets, Flurbiprofen Sodium) Members endorsed the adoption of quantitative limits for inclusion in the draft monographs, as well as the addition of a reporting threshold in line with ICH Q3B.

Flurbiprofen Eye Drops Members recommended that the monograph was considered for omission from a future edition of the BP, in the absence of active UK licensed products.

657 Bumetanide Injection (Revised) MC2(25)14

Identification The Secretariat had deleted identification test B, concordant retention time in the Assay, with IR considered sufficiently discriminatory. The IR procedure had also been updated to remove the specific use of a rotary evaporator. Members approved these changes for publication subject to stakeholder comment.

Related substances Members endorsed the drafted gradient HPLC method and limits, subject to public consultation.

Assay A test harmonised the revised Bumetanide Tablets monograph procedure due to be published in the BP 2026, which utilised isocratic HPLC, quantification at 254 nm,, was drafted by the Secretariat and approved by members, subject to stakeholder comment.

FOR INFORMATION

MC2 Work status and updates MC2(25)15

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The Secretariat presented the updated work programme to members for information.

659 BP Lab update MC2(25)16

The Secretariat reviewed the BPCRS stock for monographs relevant to EAG MC2 and presented to the group that there were no out-of-stock BPCRS.

660 Ph Eur Updates MC2(25)17

The Secretariat thanked members for their ongoing support of the Pharmeuropa review and confirmed update 37.2 was underway with public deadline of 30 June 2025.

661 ANY OTHER BUSINESS

None raised.

662 NEXT MEETING

Members were informed that the next meeting would be held virtually over two mornings in November 2025.