BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group MC1: Medicinal Chemicals

SUMMARY MINUTES

A meeting of Expert Advisory Group (EAG): Medicinal Chemicals 1 (MC1) was held in hybrid mode on Wednesday 23 July 2025.

Present: Dr P Marshall *(Chair),* Dr E Bush (*Vice-Chair*), Dr Varada Bapat, Professor D Cairns, Mr A J Caws, Mr P Fleming, Dr J Lough, Mr D Malpas, Mr S Nolan, Dr G Lee (Population Health, MHRA) and Dr F Pina (Population Health, MHRA).

In attendance: Ms G Li-Ship, Mr Darren Tong, Dr M Dmitriieva, Ms P Mandalia (CST, MHRA) Dr S Greatorex (BP Lab).

Observer: Ms H Hall (BP Commissioner).

Apologies: Dr J C Berridge, Mr S Boland.

793 Introductory Remarks

Welcome Dr Marshall welcomed all those present to the meeting and gave the attendees the opportunity to give a brief introduction of their background and experience.

Expense Claims Members were asked to note that expenses claims should be submitted electronically to committeeservicesteam@mhra.gov.uk.

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 thanked for providing their interests prior to the meeting and before discussion of each monograph item.

MINUTES OF THE PREVIOUS MEETING **MC1(25)22 & 23**

794 The minutes and summary minutes of the meeting held on 29 January 2025 were confirmed.

MATTERS ARISING **MC1(25)24**

795 Matters arising from previous meetings were noted and the group was updated on any progress.

REPORTS AND CORRESPONDENCE

796 BP Update **MC1(25)25**

Members were provided with an update on recent BP activities including the appointment of a new MHRA Chief Executive, BPC Reappointments, MC3 and MC1 Secretariat staff changes.

797 AMIODARONE PREPARATIONS **MC1(25)26**
Amiodarone Infusion (revised)
Amiodarone Tablets (revised)
Amiodarone Oral Suspension (revised)

The BP Secretariat had received a query from a user who highlighted that the Ph.Eur. 11.7 update was discontinuing amiodarone impurity E EPCRS from the Amiodarone monograph, and if the BP intended to revise the family of amiodarone monographs, which referred to this EPCRS.

Related substances Ph Eur 11.7 Amiodarone monograph update had revised the Related substances method from an isocratic to a gradient HPLC method.

Stock availability for impurity E EPCRS was expected to last only until October 2025, although it would be visible in the EDQM catalogue until the 1st April 2026 (the effective date of the 11.7).

The BP Tablets, Infusion and ULM Oral Suspension monographs all used the discontinued impurity E EPCRS in the related substances method.

In addition, two new EPCRS had been established in the revised related substances: impurity C and impurity G.

Members agreed to retain the current isocratic HPLC method and investigate the EPCRS and new system suitability requirements due to the upcoming EPCRS stock shortage.

Assay Both the BP Tablets and Infusion monographs use impurity E EPCRS for the assay test which is harmonised with the related substances test which had been based on the Ph.Eur. 9.0 (2017) update.

Members agreed to retain the current assay method and investigate the EPCRS and new system suitability requirements due to the upcoming EPCRS stock shortage.

798 PARACETAMOL PREPARATIONS: **MC1(25)27**
Paracetamol Suppositories (revised)
Paracetamol Tablets
Paracetamol Capsules
Paracetamol Dispersible Tablets
Paracetamol Effervescent Tablets
Paracetamol Soluble Tablets
Paediatric Paracetamol Oral Solution
Paediatric Paracetamol Oral Suspension
Paracetamol Oral Solution
Paracetamol Infusion

The Secretariat had received correspondence from a BP user who had requested clarification on whether to report impurity J for the Paracetamol Suppositories monograph as this contradicted the higher reporting threshold in both the BP2024 and BP2025.

The related substances method for the paracetamol family of monographs had been based on the Ph.Eur. Paracetamol monograph, which had a " – reporting threshold: not more than 0.05%, except for impurities J and K".

Due to the safety reasons, the limits for paracetamol impurities J and K had also been adopted from the Ph.Eur. drug substance monograph into the paracetamol drug product monographs.

Members agreed to the proposal to revise the reporting threshold of the BP2025 paracetamol-only monographs by adding, “except for impurities J and K”, in line with the Ph.Eur. drug substance monograph for the BP2027 edition.

799 Phenytoin Injection **MC1(25)28**

The Secretariat had received correspondence from a user requesting widening of the pH range from 11.5 – 12.1 to 11.2 – 12.1 supported by pH stability data. As part of the justification, the MAH cited compliance issues affecting continued product supply to patients and harmonising with the USP Phenytoin Sodium injection (10.0 – 12.3).

Members agreed that if there was no negative impact on the product interchangeability (as an anti-epileptic drug, AED), the change in pH to 11.2 – 12.1 could be endorsed.

800 Risperidone Oral Solution **MC1(25)29**

The Secretariat had received a BP user request to revise the pH from 2.0 – 4.0 to 1.65 – 4.00 and had submitted quality, safety and post-marketing data.

Members agreed to delete the pH test as there was no safety or quality issue, in line with the BP policy.

801 ESOMEPRAZOLE PREPARATIONS: **MC1(25)30**
Esomeprazole GR Capsules
Esomeprazole GR Tablets
Esomeprazole GR Granules
Omeprazole GR Capsules
Omeprazole GR Tablets

Dissolution

Final stage (pH 6.8) The Secretariat had received a communication from several users where. noted that the concentration of the standard solution was five times higher than that of the test solution in Esomeprazole GR capsules monograph.

This issue had also been noted for other omeprazole and esomeprazole gastro-resistant preparations and the Secretariat proposed a harmonised approach for all affected preparations, which members endorsed.

Members agreed to:

- revise the standard solution concentration to 0.001% w/v;
- revise the test solution preparation to 0.0008% w/v to harmonise with the standard solution concentration

First stage (pH 4.5)

Members agreed to:

- delete the final dilution step, which was unnecessary;
- reducing the standard solution concentration to 0.00012% w/v.

It was suggested that the determination of active ingredient at acidic stage (pH 4.5) could be omitted, with the amount of released API being controlled at the final stage (at NLT 85%).

NEW MONOGRAPHS

802 PROCYCLIDINE PREPARATIONS MC1(25)31
Procyclidine Hydrochloride
Procyclidine Tablets
Procyclidine Injection
Procyclidine Oral Solution (new)

A new monograph Oral Solution monograph had been drafted based on a MAH tablets method. The draft new monograph would be included in a future BP publication, subject to laboratory evaluation and stakeholder comment.

Draft revisions for the drug substance, Tablets and Injection monographs were presented to the group.

Minor technical and editorial comments made by members via the DRT would be considered as agreed in the meeting.

Chemical structure (API) The Secretariat agreed to correct the omitted the hydrochloride counterpart for future revisions.

Related substances (API) The Secretariat proposed adopting a GC-FID method for the related substances test, as it could detect impurity 1 as well as total impurities. The Secretariat also proposed a laboratory investigation to quantify impurity 1 and assess the accuracy of the method.

The Secretariat agreed that an internal standard would be included in the sample preparation due to the extraction, washing, and drying steps involved.

The Secretariat agreed to investigate resolution as an alternative system suitability criterion to column efficiency as peak compression would occur under a temperature gradient.

Members agreed to a proposed limit of 0.10% for individual unspecified impurities; and a limit of 0.15% for each of impurities 1 and 2, subject to laboratory evaluation or supporting data.

Assay (API) Members agreed that a limit of 98.0 – 102.0% should be used if using a GC method without using an internal standard, subject to laboratory evaluation. If the fallback option of using titration was used, the limit could be revised to 99.0 – 101.0%.

Identification (Tablets)
It was agreed that Identification Test B for chlorides would be omitted as an IR identification test was already included.

Dissolution (Tablets) The Secretariat proposed using 900 mL 0.1M hydrochloric acid as the dissolution medium with paddles rotating at 75 rpm, based on a collaborating MAH method.

Members agreed a dissolution limit of NLT 80% (Q) in 30 minutes, based on assessor feedback.

Related substances (Tablets) A HPLC method was proposed for this test, based on a collaborating MAH method.

Members endorsed testing the stability of the sample and the possibility for special sample preparation or storage conditions.

The need to use a 5° autosampler, preparing samples immediately for use whilst protection from light was also agreed to be investigated in the laboratory.

Members agreed that impurity 1 should be controlled under unspecified impurities of NMT 0.2%.

Assay (Tablets) The Secretariat proposed adopting an HPLC method for the assay, based on a validated method provided by one of the MAHs.

Members endorsed the proposal to tighten the limit to 95.0 – 105.0%.

The Secretariat agreed to investigate resolution instead of theoretical plate count during laboratory evaluation.

Identification (Injection) The Secretariat proposed using IR spectroscopy as the sole method for identification, and members endorsed the approach.

Acidity (Injection) Members agreed that the current pH requirement of 4.0 – 6.8 should be retained.

Related substances (Injection) Members endorsed the proposal of harmonising the related substances method with the one for tablets and submitting this for laboratory evaluation.

Assay (Injection) Members endorsed the proposal of harmonising the related substances method with the one for tablets and submitting this for laboratory evaluation.

Members agreed a limit of 95.0 – 105.0%, subject to public consultation.

BPCRS Review The Secretariat proposed renaming “1-phenyl-3-pyrrolidinopropan-1-one hydrochloride BPCRS” to “1-phenyl-3-pyrrolidinopropan-1-one hydrochloride BPCRS (procyclidine impurity 1)” to provide clarification to our users. Members endorsed the proposal.

	REVISION OF MONOGRAPHS	
803	**ETODOLAC PREPARATIONS:** **Etodolac PR Tablets (new)** **Etodolac Capsules**	**MC1(25)32**
	The draft new monograph would be included in a future BP publication, subject to amendments and comments from manufacturers.	
	Members agreed to propose omitting the Etodolac Capsules monograph from the BP2027 due to lack of active UK licences, and the inability to replace the dimer impurity BPCRS (Ph.Eur. impurity I) for several years, which was now out of stock, subject to stakeholder comment.	
804	**Carbimazole Tablets**	**MC1(25)33**
	Minor technical and editorial comments made by members via the DRT would be considered as agreed in the meeting.	
	Dissolution The Secretariat presented a dissolution test based on a collaborating MAH method using 500 mL of 0.1M hydrochloric acid, apparatus 2 (paddle).	
	A limit of 80% (Q) in 30 minutes was agreed, subject to laboratory evaluation and stakeholder comment.	
	Assay Members agreed to harmonise the assay test with the isocratic dissolution test, based on the collaborating MAH method, test and reference solution preparations. The laboratory would be asked to recommend a system suitability test.	
	Members agreed to revise the “Thiamazole and other related substances” and Assay tests so that any reference to the reagent “thiamazole” would reference the thiamazole EPCRS.	
805	***EUROPEAN PHARMACOPOEIA***	**MC1(25)34**
	Members were provided with an update on Ph. Eur. monographs which concerned MC1 monographs.	
	ANY OTHER BUSINESS	
806	**Alkyl Sulfonate Ester Impurities – For Information only**	**MC1(25)35**
	The background to production statements and its introduction for alkyl sulfonate ester impurities in monographs was presented to experts. An article had been circulated to members as had been agreed at a previous BP Commission meeting.	
807	**Work Programme**	**MC1(25)36**
	Members were provided a copy of the current MC1 programme to the group.	

808	**BPCRS Update**	**MC1(25)37**
	Members were provided with an update on BPCRS reports since the last meeting. There were no out-of-stock BPCRS for MC1.	
	Next Meeting	**MC1(25)38**
	TBD	