BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group BIO: Biological and Biotechnological Products

SUMMARY MINUTES

A meeting of this Expert Advisory Group was held via MS Teams on Tuesday 1st October 2024 commencing at 10:00 AM and continuing in the afternoon.

418 Introductory remarks

418.1 Welcome
The Chair welcomed everyone to the meeting.

418.2 Declaration of interests
Members were reminded to declare specific interests as they arose during the meeting and to inform the Secretariat of any changes to their interests throughout the year.

419 General matters **BIO(24)01; Annex 1**

419.1 Freedom of Information
Members were reminded that freedom of information requests should be referred to the Secretariat.

419.2 Confidentiality
Members were reminded of the confidential nature of the papers, discussions, and minutes of the meeting.

419.3 BIO membership list
Members were asked to inform the Secretariat of any changes to their contact details.

419.4 BPC Annual Report
Members were notified that the 2023 The 2023 Annual Report of the Human Medicines Regulations 2012 Advisory Bodies, which included the BP Commission's report, was published on 30th July 2024.

419.5 Organisational updates

The group were informed of organisational updates to the British Pharmacopoeia team and the wider MHRA structure.

I MINUTES

420 The minutes and summary minutes from the meeting held on 21 October 2023 were confirmed, with minor editorial revisions to be made to the summary minutes.

II MATTERS ARISING FROM THE MINUTES **BIO(24)02**

421 The following matters arising from the meeting held on 21 September 2023 were noted.

421.1 Minute 408.3 Investigation into the Removal of Animal Tests in the Iron Dextran Injection Monographs members were informed that, as discussed at the Expert Advisory Group BIO meeting

on 21 October 2023, the removal of animal products from the test method in the BP Iron Dextran Injection monograph had been implemented and was reflected in the BP 2025 edition.

421.2 **Minute 411 Bacterial endotoxin testing supplementary chapter - revision** The Secretariat discussed the request for revision for high endotoxin limits with representatives from the Ph. Eur. BET expert group and Group 12 with the agreement of presenting to the CPS group in August 2024.

421.1 **Minute 412 Heparin sodium injection - revision** An update was given to members about the additional NMR analysis with collaboration between the BP and MHRA Science Campus, on UK-marketed heparin products and the EDQM standard using the sodium heparin injection monograph.

III EAG BIO STRATEGY

422 General Update **BIO(24)03**

422.1 **New BIO memberships** New members, including lay members, joined the BP Commission in July. Additionally, four new members were appointed to the EAG BIO.

422.2 **Temporary Pause of WP-DPS Group**

422.3 **BP Website Moving to Accounts per User System** Members were briefed on the BP website's transition to an Account Per User (APU) system for multi-user licenses. This change required each user to register with an email address upon subscription renewal, with full implementation planned by the end of 2024. The transition aimed to enhance user experience and improve market research.

422.4 **Executive Summary from the 2024 BP and Labs Strategy** Members were updated on the BP & Labs Strategy for 2024-2029, which highlighted six strategic recommendations aligned with MHRA's Corporate Plan priorities. The strategy emphasised maintaining public trust through strengthened partnerships, expanding BP offerings to improve healthcare access, delivering scientific and regulatory excellence, promoting sustainable practices, and fostering a supportive environment for employee development. Progress would be monitored through metrics and stakeholder feedback.

423 Update on the progress of WP ATMP **BIO(24)04; Annexes 1-2**

423.1 **WP ATMP 6th Meeting Overview** The Secretariat provided an update from the 6th WP ATMP meeting held on 7 December 2023, a horizon-scanning paper was discussed, identifying standardisation areas in cell and gene therapies by external organisations. Experts were reminded of previously discussed topics, and two new guidance topics were proposed: “Encapsidated DNA Characterisation” and “Primary Protein Sequence Modifications,”.

423.1 **Membership Review 2023** An update was given to the increased group size.

423.2 **Replication Competent Virus Assays** Members received an update that the RCV assays subgroup intended to prepare a consultation draft for review in the near future.

423.3 **dPCR and qPCR Validation Protocols for Vector Copy Number** The Secretariat provided an update regarding the drafts of the two validation protocol and two report documents produced by the PCR subgroup, which were undergoing review.

423.4 **New subgroups** Members were informed that two new subgroups, "*Encapsidated DNA Characterisation*" and "*Primary Protein Sequence Modifications*," had been established.

IV MONOGRAPHS, CHAPTERS AND TESTS

424 Bacterial endotoxin limit investigation — BIO(24)05; Annexes 1

Following the last EAG BIO meeting, the BP Commission endorsed collaboration with the EDQM and public consultation regarding endotoxin limits. On 10 June 2024, a meeting with the Ph. Eur. Commission was held to discuss the investigation into small volume parenteral preparations. The Ph. Eur. Secretariat showed interest in collaborating and proposed submitting a revision request to relevant working groups for review. UK representatives were briefed on 4 September 2024 in preparation for discussions in upcoming meetings, emphasising the importance of gathering industry feedback on potential changes to endotoxin limits. Any proposed amendments would follow the standard public consultation process during the PharmEuropa window.

425 Heparin injection NMR Identification Test — BIO(24)06; Annexes 1-2

To verify the limit specifications, UK-marketed heparin samples, including the EDQM standard, were analysed at the MHRA Science Campus, confirming compliance with the BP Heparin Injection monograph. The investigation revealed that excipients, particularly sodium citrate, interfered with the spectral baseline in the specified range, affecting the identification peak for heparin. While not all UK-licensed products contained sodium citrate, those with lower heparin concentrations showed significant peaks, impacting the spectrum.

It was decided that the BP Heparin Injection NMR Identification test would remain unchanged since UK products met the specified limits. A list of key preservatives and buffers in UK-licensed heparin injections would be published, along with a "More Resources" section in the monograph, including a table of excipient peaks that interfere with heparin signals.

426 Multi-attribute mass spectrometry general chapter — BIO(24)07; Annex 1

A presentation on advancements in high-resolution mass spectrometry (MS) and semi-automated software led to the development of the Multi-Attribute Method (MAM) for quality control (QC) testing of therapeutic proteins. MAM allowed for the quantification of multiple product quality attributes (PQAs) within a single framework, enhancing specificity, improving product understanding, supporting Quality-by-Design (QbD) principles, and accelerating product development. However, its application in GMP settings remained limited due to regulatory challenges. MAM utilised LC-MS peptide mapping to analyse proteins, identifying product-related variants and impurities with increased sensitivity, but required further validation under ICH Q2 and specification setting under ICH Q6B for regulatory acceptance.

Discussions encouraged the inclusion of MAM in monographs, with acknowledgement to the position of the USP. The potential integration of MAM by Mass Spectrometry into the WP-DPS for developing monoclonal antibody-related monographs was considered. It was suggested that the WP-DPS group could serve as the first point of contact for this initiative, keeping abreast of developments proposed by the EDQM group. The DPS was proposed to work with existing experts to develop a document scope before involving subject matter experts. Incorporating clinically relevant specifications within

the ICH Q6 revisions was advocated for a holistic approach, with consultations involving MHRA assessors. A group similar to the ATMP groups was suggested, ensuring consideration of the USP's position. For complex generics, selecting and validating an indicator peptide, addressing background variability, and performing statistical comparisons proved challenging, necessitating consultations with the ICH Q6 MHRA representative.

427 **Desmopressin preparations** **BIO(24)08; Annexes 1-6**

A discrepancy was identified in the monographs for Desmopressin Tablets, where the active ingredient was misrepresented. Revisions were proposed to correctly describe the content as desmopressin acetate and update the content determination sections and sample preparation instructions. These changes were endorsed and would be published in the BP 2026 edition.

428 **Vaccines for human use** **BIO(24)09 Annex 1**

An update was provided on the revision of the monograph on vaccines for human use, reflecting advancements in technology and regulatory expectations. Notable updates included the addition of new vaccine classes, such as mRNA and viral-vectored vaccines, and the extension of sterility testing replacement options. The definition section was also updated to include nucleic acid-based vaccines and reorganized into specific sub-categories.

V WORK PROGRAMME AND EUROPEAN PHARMACOPOEIA

429 **Work Programme: BP Biologicals** **BIO(24)10**

Members were informed that there was one revised, no omitted, and no new BIO monographs in BP 2025. The edition was published on 1 August 2024 and would be effective on 1 January 2025.

Members were informed of the current EAG BIO work programme and were notified that current UK membership of Ph. Eur. Groups of Experts/Working Parties was available on British Pharmacopoeia website or by request from the Secretariat. This work programme was agreed to be updated following the discussions held during the meeting.

430 **European Pharmacopoeia: Biologics update** **BIO(24)11**

The group were updated on several priority work areas ongoing within EDQM and the Ph. Eur. that were related to Biologics, they were as follows:

430.1 **Alternative Rapid Microbiological Methods Workshop** The EDQM Working Party for Cell Therapy Products held a workshop to evaluate the feasibility of a certification system for rapid microbiological methods, specifically rapid sterility tests.

430.2 **mAb Questionnaire Responses** EDQM published the Monoclonal Antibody Stakeholder Engagement Survey, with feedback collected in October/November 2023 from groups such as South Mimms and WP BIO-DPS. The survey aimed to inform the Ph. Eur.'s strategy for monoclonal antibody monographs and chapters.

430.3 **Bacteriophages Working Party** The Ph. Eur. Commission adopted a new general chapter on phage therapy medicinal products for human and veterinary use (5.31), highlighting its role in combating antimicrobial resistance.

430.4 **PharmEuropa** PharmEuropa 36.3 remained open for public comment until 30 September 2024. The BP team circulated drafts for input on documents related to Ustekinumab, Golimumab, Alteplase, human albumin, and diphtheria vaccines. Comments were encouraged for submission to EDQM.

430.5 **Questionnaires Sent to the UK National Authority** The Secretariat consulted BP experts and the UK delegation over the past year on BIO-related surveys, resulting in the adoption of suppressions for gene transfer medicinal products, Hepatitis A vaccine (inactivated, virosome), and Influenza vaccine (whole virion, inactivated).

VI ANY OTHER BUSINESS

431 An expert enquired about using prescription data to inform which monographs should be elaborated within the EAG BIO work programme going forward. It was explained that this activity was taken up at Commission level.

432 The next meeting would be scheduled for Autumn 2025 and would be held in person.

Expert Advisory Group: Biologics and Biotechnological Products

List of Acronyms/Synonyms for use by BP Secretariat

Acronym/Synonym	Name
AAV	Adeno Associated Virus
APVMA	Australian Pesticides and Veterinary Medicines Authority
ATMP WP	Advanced Therapy Medicinal Products Working Party
AQbD	Analytical Quality by Design
BAN	British Approved Name
BIO-DPS WP	Alternative Approaches for Documentary and Physical Standards for Biotechnological Products Working Party
BP	British Pharmacopoeia
BP (Vet)	British Pharmacopoeia (Veterinary)
BPC	British Pharmacopoeia Commission
BPCRS	British Pharmacopoeia Chemical Reference Substance
BRP	Biological Reference Preparation
BSP	Biological Standardisation Programme
CAR	Chimeric Antigen Receptor
CHM	Commission on Human Medicines
CRS	Chemical Reference Substance
EAG	Expert Advisory Group
EDQM	European Directorate for the Quality of Medicines & HealthCare
EPBRP	European Pharmacopoeia Biological Reference Preparation
EPC	European Pharmacopoeia Commission
EPCRS	European Pharmacopoeia Chemical Reference Substance
EU	European Union
FIP	International Pharmaceutical Federation
FOI	Freedom of Information
GC	Gas chromatography
ISO	International Organisation for Standardisation
LC	Liquid chromatography
LD	Licensing Division
LGC	Laboratory of the Government Chemist, Teddington
LR	BP Laboratory Report
MAB WP	Monoclonal Antibody Working Party
MAH	Market Authorisation Holder

MHRA	Medicines and Healthcare products Regulatory Agency
NIBSC	National Institute for Biological Standards and Control
NOAH	National Office of Animal Health
NPA	National Pharmacopoeial Authority
OMCL	Official Medicines Control Laboratory
Ph. Eur.	European Pharmacopoeia
SC	Supplementary Chapter
SCB	Standards Coordinating Body for Regenerative Medicines
TGA	Therapeutic Goods Administration, Australia
TLC	Thin layer chromatography
UK	United Kingdom
UKD	United Kingdom Delegation [to the European Pharmacopoeia]
USP	United States Pharmacopeia
VMD	Veterinary Medicines Directive
WHO	World Health Organisation