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 Thursday 21st September 2023 commencing at 10:00 AM and continuing in the afternoon.

Present: Anna-Maria Brady (Chair), Emre Amirak (Vice Chair), Ben Cowper, Meenu Wadhwa, Sean Jones, Chris Burns, Brij Patel, Lincoln Tsang, Robin Thorpe, and Simeon Gill.

Apologies: *Alistair Kippen, Vincent Loh, Cassandra Braxton, Paul Varley, and Louise Bisset.*

In attendance: Ryan Smith, Carolyn Swann, Kajetan Rakowski, Sarah Bowles, and Munise Guler.

404 Introductory remarks

404.1 **Welcome**
The Chair welcomed everyone to the meeting.

404.2 **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.

405 General matters **BIO(23)01; Annex 1**

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

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

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

405.4 **Organisational updates**

The Secretariat informed members of notable MHRA/BP activity since the last meeting of EAG BIO.

406 Membership review 2023 **BIO(23)02**

The Secretariat informed the attendees that the term of office for all current members of the Expert Advisory Groups, Panels of Experts, and Working Parties of the BP Commission had been scheduled to end on the 31st December 2023. He mentioned that a call for expressions of interest had been released on the BP website and MHRA media channels.

I MINUTES

407 The minutes and summary minutes of the meeting held on 22nd September 2022 were confirmed.

II MATTERS ARISING FROM THE MINUTES

408 The following matters arising from the meeting held on 22nd September 2022 were noted.

408.1 South Mimms Collaboration on ATMP Work

408.2 Revision of the Protamine Sulphate Injection Monograph

408.3 Investigation into the Removal of Animal Tests in the Iron Dextran Injection Monographs

III EAG BIO STRATEGY

409 General Update BIO(23)03

The Secretariat began by stating that there had been no changes to the strategy since the last EAG BIO meeting. He emphasised that the primary focus continues to be on WP ATMP non-mandatory guidance and the exploration of alternative standards for monoclonal antibodies. The specific details for each project were covered later during the meeting.

410 Update on the progress of WP ATMP BIO(23)04

Members received a verbal update on the activities of the WP ATMP since EAG BIO last met in September 2022. Two new subgroups have been established: Replication-competent virus assays and Validation protocols and reports for digital and quantitative polymerase chain reaction for vector copy number. Two public consultations have run and concluded, one for the Characterisation of particle population for AAV products (empty capsids), and one for T cell and NK cell characterisation assays. All comments received during the public consultations had been addressed and the finalised versions of the documents have been passed over to the BP's third-party publisher.

411 Update on the progress of BIO-DPS WP BIO(23)05

The Secretariat presented a verbal update on the completed WP-DPS Round Robin, which examined glycosylation results from both the example and in-house methods.

IV MONOGRAPHS, CHAPTERS AND TESTS

411 Bacterial endotoxin testing supplementary chapter - revision BIO(23)06

The group heard updates during the meeting about concerns about the clinical safety-based acceptance criteria not including a safety margin, contrary to GMP principles. This omission could pose hidden safety risks for certain products. The following actions were proposed:

a) Including more detailed guidance for specific medicine presentations in the BP SC I. This could involve specifying an upper limit for endotoxin concentration, subject to public consultation, and adding a line to SC I C stating, "Higher values, in compliance with SC I C. ANNEX, to be justified." An example was given using Flucloxacillin with a limit of 750 EU/mL.

b) Reviewing BP monographs (fifty-nine injection monographs) that include an endotoxin test to assess appropriate limits. The BP Secretariat would conduct the review and collaborate with expert groups responsible for these monographs.

412 Heparin sodium injection – revision BIO(23)07

Members were informed of a query from a pharmaceutical company. The company identified the ^{1}H NMR ID limit of the ratio of peak signals at 2.11ppm and at 5.42ppm for sodium heparin injection for the NMR range was out of specification when the analysis was performed on three batches of EU-marketed finished products including the EDQM reference material. The company found the unidentified signals from all products generated a higher ratio, between 4.9-15.8%, than the specified limit (4%) stated in the monograph.

413 Oxytocin injection – revision BIO(23)08

During the meeting, several proposals were made. These included changing the column to a high-resolution one and adjusting the injection volume to match the drug substance monograph. The possibility of reducing the injection volume from 200 microliters to 50 microliters was discussed. There was also a proposal to explore the use of a new column for the monograph and initiate lab work. The injection volume was to be recalculated based on the new column. Additionally, investigating a column capable of handling a higher injection volume, potentially involving longer column dimensions, was suggested. The group recommended modifying the way column parameters are specified in the monograph to enhance clarity for readers in selecting different columns.

414 Enoxaparin Sodium Injection BIO(23)09

Members were made aware that a new monograph for Enoxaparin Sodium Injection had been prepared for inclusion in the European Pharmacopoeia. The BP currently contains a national Enoxaparin Sodium Injection monograph which would be superseded by the Ph. Eur. monograph if it were to be adopted. Members discussed the differences between the two monographs, in particular the lack of a Related substances test in the Ph. Eur. monograph. It was noted that the Ph. Eur. text cross-referring to other monographs such as the Enoxaparin Sodium API monograph, which itself cross-refers to the Low-Molecular Weight Heparins monograph, should eliminate the possibility of contamination in Enoxaparin Sodium Injection products. Members agreed that the Ph. Eur. monograph should be adopted into the BP.

V WORK PROGRAMME AND EUROPEAN PHARMACOPOEIA

415 Work Programme: BP Biologicals BIO(23)10

Members were informed that five revised BIO monographs had been included in the BP 2024 and one BIO monograph had been omitted. The edition was published on August 1st 2023 and would be effective on 1st January 2024. The monographs included in BP 2024 had been discussed at the 2022 meeting of EAG BIO.

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.

416 European Pharmacopoeia: Biologics update BIO(23)11

The group were updated on several priority work areas ongoing within EDQM and the Ph. Eur.

416.1 **Monoclonal antibody stakeholder engagement**

The UK Delegation (UKD) formally clarified and requested monoclonal antibody stakeholder engagement during EPC 175; UKD sent a letter on 19 May 2023 and, EDQM responded with an acceptable proposal for a survey in Pharmeuropa 36.1, scheduled to appear during January to March 2024 and will focus on the scope of the mAb pilot phase and profiling of the responder. BP had received a draft version of the survey, which can now be circulated to interested parties for review. The specific content of the survey will be formally approved during EPC 177 (November 2023).

416.2 **mRNA vaccines group**

A newly established group for mRNA has two UK representatives. General chapters for mRNA Drug Substance and mRNA-lipid nanoparticles Drug products are under consideration. Specific monographs for excipients will be included where required.

Bacteriophages

416.3 The general chapter "5.31 Phage therapy active substances and medicinal products for human and veterinary use" was drafted and published in Pharmeuropa 35.2 for public consultation.

VI ANY OTHER BUSINESS

417 The next meeting would be scheduled for Autumn 2024

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