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 22nd September 2022 commencing at 10:00 AM and continuing in the afternoon.

Present: Anna-Maria Brady (Chair), Emre Amirak (Vice Chair), Ben Cowper, Robin Thorpe, Brij Patel, Chris Burns, Lionel Randon, Vincent Loh, Simeon Gill, Silke Schepelmann, Lincoln Tsang, Louise Bisset, Peter Rigsby (Invited expert), Eleanor Atkinson (Invited expert)

Apologies: *Anne Cook, Chris Jones, Alistair Kippen, Paul Varley, Meenu Wadhwa*

In attendance: Ryan Smith, Carolyn Swann, Kajetan Rakowski

387 Introductory remarks

387.1 **Welcome**
The Chair welcomed everyone to the meeting and introduced Carolyn Swann, a new starter to the BP and Kajetan Rakowski (Kai) who was due to join the team in October and observed the meeting. The group introduced themselves and areas of interest to one another.

387.2 **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.

387.3 **Use of Teams**
Mr R Smith gave a brief outline of how to use MS Teams functionality during the meeting.

388 General Matters **BIO(22)01; Annex 1**

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

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

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

388.4 **Organisational updates**

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

I MINUTES

389 The minutes and summary minutes of the meeting held on 22nd September 2021 were confirmed.

II MATTERS ARISING FROM THE MINUTES

390 The following matters arising from the meeting held on 22nd September 2021 were noted.

III EAG BIO STRATEGY

392 General Update **BIO(22)02**

The Secretariat updated members on the ongoing implementation of the MHRA's strategy for pharmacopoeial quality standards for biological medicines.

393 Update on the progress of WP ATMP **BIO(22)03; Forum**

Ryan Smith gave a verbal update on the activities of WP ATMP since EAG BIO last met in September 2021: two of the ATMP guidance documents had been published on the British Pharmacopoeia website. The flow cytometry and vector copy number guidance had been well received. There had been approximately 300 unique downloads of the documents from 26 countries.

The empty capsids guidance was at an advanced stage of review and was almost ready for public consultation.

ACTION BP Secretariat to follow up with Chris Burns and NIBSC colleagues around collaboration on new WP ATMP subgroups

394 Update on the progress of BIO-DPS WP **BIO(22)04; Annexes 1-2, Forum**

Carolyn Swann gave a verbal update including a background of the WP- DPS study focussing on the glycosylation data from the five participating laboratories performing both 'example' and 'in house' methods using the same supplied material. Initial comparison of the results between the laboratories were shown in a data table presented and displayed the total afucosylated and main glycan peaks.

ACTION BP Secretariat to follow up with Biostats colleagues at NIBSC, Peter Rigby and Eleanor Atkinson after official statistical analysis has been completed and the finding will be shared with the group once meaningful conclusions from the data have been extracted.

IV MONOGRAPHS

395 Bacterial endotoxin testing Supplementary Chapter - Revision **BIO(22)05; Annexes 1 – 4**

Members were informed of the technical details of a revision relating to Supplementary Chapter XIV C. Some updates were proposed from a previous BPC meeting. The Secretariat were particularly interested in the equivalence of the rFC and LAL test as users would now have the option to choose between the two tests under the new policy. EAG BIO members endorsed the proposals.

396 Biphasic insulin aspart injection - revision **BIO(22)06; Annexes 1 – 2**

Members were informed of a query from the manufacturer regarding the equation for determination of content and the possibility that the values were incorrect. Further investigation displayed in annex 1 showed that the text in the protocol was incorrect asking the test user to repeat the addition of 50 mL of tris/EDTA buffer. This error in the text had been corrected using the manufacturer method.

ACTION **Members endorsed the revision for publication in BP 2024**

397 **Biphasic insulin lispro injection – revision** **BIO(22)07; Annexes 1 - 2**

Members were informed of a query from the manufacturer stating that there was an incorrect limit of 1.5% for Impurities with molecular masses greater than that of insulin (HMWP) and this should be revised from 1.5% to the licensed limit of 3%.

398 **Heparin injection - revision** **BIO(22)08; Annexes 1-3**

This item was for information only and had already been agreed via e-mail correspondence earlier in the year. A short discussion was held about rectifying a disregard limit for heparin injection. In the BP 2020 the disregard limit was mistakenly set at 0.02%, to reflect the drug substance monograph.

399 **Protamine sulfate injection - revision** **BIO(22)09; Annexes 1-3**

The group indicated that the Assay test should be rectified. The content limit was based on the Assay and as currently written the Assay instructed analysts to carry out a Potency Assay. EAG BIO agreed that the Assay method should instead be based on the Protein Assay.

ACTION **The BP Secretariat took an action to revise the protamine sulfate monograph, specifically to change the test indicted under Assay from a potency assay to a protein assay.**

400 **Removal of Miscellaneous Animal Testing** **BIO(22)10**

Iron Dextran Injection - Undue Toxicity (*also known as innocuity test, abnormal toxicity test or general safety test*) and Iron Absorption. The group were unaware of suitable alternatives for these tests and advised the secretariat to contact the MAH for further information.

Erythropoietin Injection - Assay (In polycythaemic mice and In normocythaemic mice). The group agreed that this test must remain in the Pharmacopoeia as there are no viable in vitro alternatives to test the mechanism of action of Erythropoietin.

Streptokinase Injection – Identification. The group agreed that no alternatives were available for this animal assay.

V **WORK PROGRAMME AND EUROPEAN PHARMACOPOEIA**

401 **Work Programme: BP Biologicals** **BIO(22)11**

Members were informed that two revised BIO monographs had been included in the BP 2023, one BIO monograph had been omitted. The edition was published on August 1st 2022 and would be effective on 1st January 2023. The monographs included in BP 2023 had been discussed at the 2021 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.

402 European Pharmacopoeia: Biologics update BIO(22)12

402.1 **Monoclonal antibodies**

The group were informed that the UK delegation has considered the proposals on the general chapter on 'Cell-based assays for potency determination of TNF-alpha antagonists (2.7.26)' and revised monographs Infliximab concentrated solution and Etanercept. The group were reminded of the previous concerns of the UKD over the Ph. Eur. monoclonal antibody work and that further monoclonals had been added to the work programme.

402.2 **Gene Therapy Products – Gene therapy medicinal products for human use**

It was brought to the attention of the group that a general monograph for Gene therapy medicinal products for human use and the general chapter Additional information on gene therapy medicinal products for human use were published in PharmEuropa 34.3 for comment.

402.3 **Gonadotrophin, equine serum, for veterinary use**

A conclusion was given to the group around the omission of serum gonadotrophin and members were reassured that this would have minimal impact on the products on the UK market, as discussed at the beginning of the meeting.

402.4 **Pyrogenicity**

Please refer to Minute 384.4

402.5 **Bacteriophages**

The group were reminded that a general chapter for "Phage therapy active substances and medicinal products for human and veterinary use" continued to be drafted.

VI ANY OTHER BUSINESS

403 The next meeting would be scheduled for Autumn 2023, two proposed dates of 14th and 28th September were agreed upon.

ACTION The Secretariat to send a placeholder for EAG BIO 2023.

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