BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group BIO: Biological and Biotechnological Products

SUMMARY MINUTES

A meeting of the Expert Advisory Group was held at 10 South Colonnade, Canary Wharf, London E14 4PU on Friday 13th September 2019.

Present: Dr P Varley (*Chair*), Mr S Gill, Dr B Patel, Mr L Randon, Dr R Thorpe, Dr V Loh, Dr C Burns, Dr A Kippen, Dr B Cowper and Dr L Tsang.
Dr T Rudd contributed to the meeting by teleconference for item BIO(19)07.

In attendance: Mr A Gibb, Dr G Kemp, Dr H Bowden and Mr S Maddocks.

Apologies for absence were received from Dr A M Brady, Dr W Zunic and Mr P Sheppard.

Opening Remarks

Welcome The Chair welcomed everyone to the meeting including new members: Dr Cowper and Dr Loh. It was also noted that it was Dr Kippen's first meeting as a full member (he was previously a specialist member). The Chair noted that Dr Gardiner had moved roles within the Agency since the Group's last meeting.

Declaration of Interests The Chair asked members to declare any interests at the start of the meeting and prior to the relevant agenda item.

341 General Matters BIO(19)01

Organisational updates The Secretariat informed members that the CEO of the MHRA, Dr Ian Hudson, was stepping down on the 20th September 2019 and that Dr June Raine would take over as interim CEO until a permanent successor was announced. Dr Raine had been the Director of the MHRA's Vigilance and Risk Management Division.

The Secretariat also informed members of the recruitment of new British Pharmacopoeia Commission members by the Cabinet Office. Applications were open until 4th of October and members were encouraged to speak to the Secretariat for more information if interested.

I MINUTES

342 The minutes of the meeting held on 7th September 2018 were confirmed.

II MATTERS ARISING FROM THE MINUTES

343 It was noted that all items arising from the minutes of the meeting of EAG BIO held on 7th September 2018 had been accounted for within the papers, except for the further detail on the laboratory risk assessment procedure which was to be provided at a future meeting.

III EAG BIO STRATEGY

344 MHRA Strategy for Pharmacopoeial Quality Standards for Biological Medicines

General update and ATMPs BIO(19)02

The Secretariat updated members on the implementation of the MHRA's strategy for pharmacopoeial quality standards for biological medicines. The update included progress made regarding understanding the specific needs for standardisation in the advanced therapy medicinal products (ATMPs) field. The Secretariat noted how the work supported wider government initiatives, including the Life Sciences Industrial Strategy. In addition, it supported the Agency's Corporate Plan which included objectives to promote innovation and supported production of higher quality medicines. The Secretariat were engaging heavily with international stakeholders to ensure the relevance and direction of the strategy. Members noted the unique position of the Agency to explore biological standards, since the Agency had the regulator (MHRA), biologics expertise (NIBSC) and standards expertise (BP) within the same organisation.

Update on the progress of BIO-DPS WP BIO(19)03

The Secretariat updated the group on progress of the BIO-DPS working party noting that the working party had been established to explore the potential value of performance and class-based concepts in assuring the quality of biological medicines and enabling and supporting innovation.

IV MONOGRAPHS IN PROGRESS

345 Erythropoietin Injection BIO(19)04

Members were reminded that the replacement of the BRP with two new EPCRS in the monograph had been discussed at the previous meeting. Members had endorsed the change in principle but recommended that laboratory work should be carried out the confirm its suitability.

Identification B The Secretariat informed members that NIBSC had carried out the method using the Erythropoietin for physicochemical tests EPCRS on two previous occasions during establishment of the CRS and confirmed its suitability at the stated concentration.

Dimers and related substances of higher molecular weight – method A The use of the BRP had been substituted for the Erythropoietin for SEC system suitability EPCRS, and its suitability was confirmed in the NIBSC laboratory. Members agreed with the proposed changes.

Dimers and related substances of higher molecular weight – method B The use of the BRP had been substituted for the Erythropoietin for SEC system suitability EPCRS, and its suitability was confirmed in the NIBSC laboratory with some minor method amendments. Members agreed with the proposed changes.

346 Oxytocin Injection BIO(19)05

At the last meeting, the group had been informed that the Oxytocin Injection monograph should undergo revision. Manufacturers had been contacted and methods for the tests obtained. Members confirmed that the methods should be evaluated in the laboratory.

Members noted the possibility of adding a test for acetates in the Identification section. The Secretariat agreed to investigate.

Related substances The proposed method was found to be suitable by the BP Laboratory with modifications. 5 out of 6 manufacturer products had been tested, the one product not tested had a very similar formulation to those tested and so it had been concluded that the method would be suitable. Members agreed to inclusion of the method.

Assay The proposed method was found to be unsuitable for all products by the BP Laboratory due to excipient interference. The Related substances method was found to be suitable by the BP Laboratory with modifications. 5 out of 6 manufacturer products were tested, the one product not tested had a very similar formulation to those tested and so it had been concluded that the method would be suitable. Members agreed to inclusion of the method.

347 Ergometrine and Oxytocin Injection BIO(19)06

At the last meeting, members recommended that the Ergometrine and Oxytocin Injection monograph should undergo revision. As there was only one manufacturer of the product, members recommended including the method without laboratory evaluation.

Related substances The HPLC method from the sole manufacturer was included. Members agreed with inclusion of the method.

Assay – for oxytocin The HPLC method from the sole manufacturer was included. Members agreed with inclusion of the method.

348 Heparin Injection BIO(19)07

The revision of the Heparin Injection monograph had been discussed at the last EAG BIO meeting, where it had been highlighted that the current Identification C method, utilising zone electrophoresis, should be updated. Members suggested investigating use of the NMR method utilised in the Ph. Eur. API monographs (Heparin Calcium and Heparin Sodium).

The NIBSC laboratory completed experiments assessing the suitability of the method and early results were promising, however further work was needed before a monograph could be presented for adoption. Further work included: a review of excipients found in all licensed products, analysis of Heparin calcium for NMR identification using the proposed method and consideration of the details to include in the monograph.

Members agreed to the further work proposed on the monograph and that a monograph could be adopted by correspondence if a draft can be produced in time for publication in the BP2021.

VII WORK PROGRAMME AND EUROPEAN PHARMACOPOEIA

349 Work Programmes: BP and Ph. Eur. Biologicals Update BIO(19)08

BIO monographs included in the BP2020 Members were informed that five revised and three omitted BIO monographs had been included in the BP2020. The edition was published on August 1st and would be implemented on 1st January 2020.

Work Programmes The work programmes of the expert group, as well as the relevant European Pharmacopoeia expert groups had been included in the papers for the meeting.

350 European Pharmacopoeia: Pharmeuropa BIO(19)09

Relevant comments were highlighted to members.

351 Texts adopted at the 162nd, 163rd and 164th Sessions BIO(19)10

Lists of the documents relevant to the Group that had been adopted at the EPC over the past year were provided to members for information.

352 European Pharmacopoeia – Biologics Update BIO(19)11

Members discussed the European Pharmacopoeia's two pilot phases investigating biopharmaceutical finished product monographs and monoclonal antibody monographs.

Members highlighted the importance of evaluating the impact of current monographs for biological products, particularly on regulatory processes. Members also noted the work of BIO-DPS WP as a key exploratory study into alternative approaches that may offer different options to overcome challenges in the standardisation of biological products.

353 BP Portfolio Review BIO(19)12

A set of general principles and measures had been developed by the Secretariat to support a broad and systematic review of the BP portfolio. Revision or omission of monographs had previously been identified through the course of EAG work and largely on an ad-hoc basis. The implementation of a systemic and regular review across the BP's standards portfolio was ongoing and would ensure that resource was focussed where the MHRA could bring the most value to public health.

354 Groups of Experts: Formal reports BIO(19)13

Members noted that if they wished to receive previous reports the Secretariat should be informed.

VIII ANY OTHER BUSINESS

Date of Next Meeting: to be announced.

List of Acronyms/Synonyms for use by BP Secretariat

Acronym/Synonym	Name
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
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
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
TGA	Therapeutic Goods Administration, Australia
TLC	Thin layer chromatography
UK	United Kingdom
UKD	United Kingdom Delegation [to the European Pharmacopoeia]

USP	United States Pharmacopeia