BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group BIO: Biological and Biotechnological Products

SUMMARY MINUTES

A meeting of the Expert Advisory Group was held at 151 Buckingham Palace Road, Victoria, London SW1W 9SZ on Monday 7th November 2016.

Present: Dr P Varley (*Chair*), Dr A M Brady, Dr A Bristow, Prof D H Calam, Mr S Gill, Dr B Patel, Mr L Randon, Mr P Sheppard, Dr A Thomas, Dr R Thorpe

Dr C Burns contributed to the meeting by teleconference

In attendance: Mr A Gibb, Dr R A Pask-Hughes, Dr A Gardiner

Apologies for absence were received from Dr L Tsang (*Vice-chair*), Mr T Pronce, Dr E Griffiths, and Dr T Sesardic.

Opening Remarks

Welcome The Chair welcomed everyone to the meeting, in particular new member Dr Brady. Members introduced themselves and gave brief overviews of their background experience in relation to the work of the EAG.

Comments had been received from Dr T Sesardic and these were taken into consideration during the discussions and decisions of the relevant agenda items.

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

Mr Randon, Dr Varley and Dr Patel declared an interest in one or more agenda items and appropriate action was taken.

286 General Matters BIO(16)01

Emergency exit The emergency evacuation procedure was confirmed.

BIO membership list Members were asked to inform the Secretariat of any changes to their contact details. The current contact details were circulated for checking at the meeting.

I MINUTES

287 The minutes of the meeting held on 18th November 2015 were confirmed.

II MATTERS ARISING FROM THE MINUTES

288 A list of matters arising from the minutes of the meeting of EAG BIO held on 18th November 2015 was provided. A copy is attached.

III EAG BIO STRATEGY AND WORK PROGRAMME

289 Strategy update BIO(16)02

A verbal update on the progress made towards implementation of the strategy and development of a public consultation document was presented by the Secretariat.

290 Monograph Approaches BIO(16)03

Presentations were given related to different approaches and perspectives to monograph development for biologicals.

291 BIO Work Programme BIO(16)04

BP 2016 The new and revised texts relating to the work of the EAG that had been included in the BP 2016 were noted, in particular, four new monographs and four technically revised monographs.

Current work programme The current BP BIO work programme was noted.

European Pharmacopoeia The current work programmes for Ph. Eur. Groups of Experts 6 and 15 and Working Party P4BIO that were related to the work of EAG BIO were noted. Supplements 8.7, 8.8 and 8.9 of the Ph. Eur. had been published and were being progressively incorporated into the BP online through in-year updates. The new Ph. Eur. CTP chapter entitled Raw materials of biological origin for the production of cell-based and gene therapy medicinal products (5.2.12) was noted.

IV NEW MONOGRAPHS

292 Heparin Flush Solution BIO(16)05

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

293 Biphasic Insulin Aspart Injection BIO(16)06

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

294 Biphasic Insulin Lispro Injection BIO(16)07

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

295 Follitropin for Injection BIO(16)08

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

296 Terlipressin Injection BIO(16)09

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

V MONOGRAPHS IN PROGRESS

297 Follitropin Injection BIO(16)10

The draft monograph would be included in a future BP publication, subject to comments from manufacturers.

VI REVISION OF MONOGRAPHS

298 Goserelin Implants BIO(16)11

The monograph had been revised to include an additional orthogonal Identification test, referencing the Uniformity of Content test. The change was endorsed by the group.

299 Pancreatin Capsules BIO(16)12

Members were reminded that a Pancreatin Capsules monograph had been published in the BP2017 with a requirement to carry out a dissolution test stipulated in the production section, with the agreement that the Secretariat would request information from manufacturers regarding their dissolution methodology.

Available products The Secretariat reported that there were four pancreatin capsule products available, and that three of these were gastro-resistant but that the manufacturer of the fourth had confirmed that their product was not gastro-resistant. Members were asked whether the monograph should be re-named Gastro-resistant Pancreatin Capsule. This course of action was endorsed and it was noted that it would be more transparent to users.

Dissolution methodology Methodology for a dissolution test which measured the lipase activity of the product had been received from a manufacturer and was discussed by the group.

Members were asked whether the approach was appropriate for pharmacopoeial dissolution testing as the methodology was unusual. It was concluded that the advice of EAG PCY should be sought on the matter before a decision was reached.

Test for Gastro-resistance The manufacturer had also provided a disintegration test for gastro-resistance. A requirement for disintegration testing for gastro-resistant tablets was already included in the Tablets general monograph, therefore it was agreed not to include the test in the monograph.

300 Gastro-resistant Pancreatin Tablets BIO(16)13

Members were informed that during the stakeholder consultation prior to the publication of the Pancreatin Capsules monograph, a comment was received from a manufacturer proposing that Identification A be replaced with a reference to the test for protease activity to eliminate the use of the carcinogenic reagent congo red fibrin. The change had been accepted by the group. Members were asked whether the same amendment should be made to the Gastro-resistant Pancreatin Tablets monograph; the change was endorsed.

301 Viral Safety Of Urine Derived Materials BIO(16)14

It had previously been agreed that once the EMA Guideline for the adventitious agent safety of urine-derived medicinal products had been adopted and the revisions to the affected Ph. Eur. monographs had been proposed, any changes required to BP monograph for Menotropin would be considered. The Secretariat reported that the guideline had been published and that the three Ph. Eur. revisions were available for comment as part of Pharmeuropa 28.3. The monographs contained an amended production section and the relevant tests had been removed. The Menotrophin monograph had been amended in line with the Ph. Eur. revisions. The group were asked to discuss the implementation of the guideline and the monograph revisions.

Members raised concerns that the guideline was more encompassing of risk considerations involved in removing the tests than was portrayed in the revisions. The Secretariat undertook to investigate whether further information regarding the tests would be published elsewhere in the European Pharmacopoeia.

VII REPORTS AND CORRESPONDENCE

302 Insulin Lispro Injection BIO(16)15

Members were informed that a request for revision had been received from the sole MAH of Insulin Lispro Injection. They had requested that the limits section in the Test for Related Proteins be amended to remove the ‘any other impurity’ limit. A member of the group undertook to examine the information provided to determine whether the request was supported.

VIII EUROPEAN PHARMACOPOEIA

303 Comments from the British Pharmacopoeia Commission BIO(16)16

Members noted that comments from the BP Commission had been sent to Strasbourg on proposals for new and revised Ph. Eur. texts included in Pharmeuropa Volumes 27.3, 28.1 and 28.2.

304 Comments requested from members on draft texts BIO(16)17

Members were reminded that comments on draft texts included in Pharmeuropa Volume 28.4 should be submitted by 31 December 2016 either by using the BP Website forum or contacting the Secretariat directly.

305 Texts adopted at the 153rd, 154th and 155th Sessions BIO(16)18

Lists of the documents relevant to the Group that had been adopted at the 153rd, 154th and 155th Sessions of the EPC were provided to members for information.

306 Groups of Experts: Formal reports BIO(16)19

The most recently available formal reports and summaries of decisions of Groups of Experts 6 and 15, and Working Parties BET, CTP, RCG, MAB and P4BIO had been made available to members electronically. Members noted that if they wished to receive previous reports the Secretariat should be informed.

IX ANY OTHER BUSINESS

Date of Next Meeting: to be announced.

British Pharmacopoeia Commission
Panel of Experts BIO: Biological and Biotechnological Products

II – MATTERS ARISING

Matters arising from the Minutes of meetings held 6th November 2014 and 18th November 2015
(other than those appearing on the Agenda)

Minute 201	**Similar Biological Medicinal Products (Biosimilars)**	The Secretariat are to investigate what changes are necessary to the BP guidance in the Supplementary Chapter III B (Monograph Development: Mechanisms) and Supplementary Chapter IX (Similar Biological Medicinal Products) following the replacement of the UK specific Black Triangle Scheme with the EU Additional Monitoring Scheme.
Minute 236	**Insulin Glargine Injection**	Investigation is still ongoing on if any change is required to Solution (3) of the test for Impurities with molecular masses greater than that of Insulin Glargine following comments from the manufacturer. The questions concerned the concentration to be used for disregard and the concentration of acid.
Minute 246	**Enoxaparin Sodium Injection**	Investigation into whether additional sample preparation and method details are required in the test are still ongoing. A comment has also been received from a BP Commission member stating that the test solution concentration for the test for Light absorption was too concentrated. This is also undergoing checking from the Secretariat.
Minute 247	**Insulin Aspart Injection**	The query concerning inclusion of an appropriate disregard limit in the test for Related proteins has been raised with the manufacturer. They responded that this was not necessary.
Minute 262.4	**Live Biotheraputic Products Working Party**	A colleageu at Public Health England has been contacted concerning probiotics and a response is awaited. Further consultations have yet to be undertaken within the MHRA and Food Standards Agency.

Minute 265	**Vaccine Abbreviations**	The agreed abbreviation Flu (Live, Nasal) for Influenza Vaccine (Live, Nasal) has been brought to the attention of the head of Immunisation Hepatitis & Blood Safety, Public Health England. The Secretariat is to arrange for discussions with PHE with the intentions of explaining the background and development of the BP abbreviations and an abbreviation for the influenza vaccine.
Minute 266	**Danaparoid Sodium**	The monograph publication has been put on hold whilst the Ph. Eur. investigate a suitable replacement for the test for chondroitin sulphate and dermatan sulphate, following the discontinuation of the required enzyme.
Minute 280	**Collaboration with other Pharmacopoeias**	Discussions with other pharmacopoeias on collaborative work to produce harmonised monographs is continuing.
Minute 285	**Erythropoietin request for revision from NIBSC**	The UK request was accepted at the 153rd Session and considered by the Group 6. A Biological Standardisation Programme study has been undertaken to establish the proposed SEC system suitability CRS. This has been endorsed by the appropriate committees.

List of Acronyms/Synonyms for use by BP Secretariat

Acronym/Synonym	Name
BAN	British Approved Name
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
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