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 Wednesday 18th November 2015.

Present: Dr L Tsang (*Chair*), Dr A Bristow (*specialist*), Prof D H Calam, Mr S Gill, Dr E Griffiths, Dr B Patel, Dr P Stickings (*specialist*), Dr A Thomas, Dr R Thorpe, Dr C Burns.

Dr P Varley (*Vice-chair*) contributed to the meeting by teleconference.

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

Dr P Holland attended the meeting for item BIO(15)03 and Ms A Gardiner attended the meeting as an observer.

Apologies for absence were received from Mr T Pronce, Mr L Randon, Dr T Sesardic and Mr P Sheppard.

Opening Remarks

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

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.

I MINUTES

259 The minutes and summary minutes of the meeting held on 6th November 2014 were confirmed.

II MATTERS ARISING FROM THE MINUTES

260 A list of matters arising from the minutes of the meeting of EAG BIO held on 6th November 2014 was provided. A copy is attached.

Vaccine Abbreviation (minute 235) The proposed dTaP abbreviation for Diphtheria, Tetanus and Pertussis (Acellular Component)Vaccine (Adsorbed, Reduced Antigen(s) Content) had been accepted by the immunological section of the Department of Health and included in the BP 2016.

Bovine Heparin (minute 238) Information was being sought on the need for development of a monograph.

III REPORTS AND CORRESPONDENCE

261 General Matters BIO(15)01

Emergency exit The emergency evacuation procedure was confirmed.

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

BIO membership Members noted that as the term of office for all members of EAG BIO had ended on 31st December 2014, a review of membership had taken place. Following the review, 13 full members and 12 specialist members had been appointed for a period of 4 years.

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

262 Work Programmes: Ph. Eur. and BP Biologicals Update BIO(15)02

Work Programme The current BP BIO work programme was noted.

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 the new monograph for Interferon Beta-1a Injection and 4 technically revised monographs.

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 8.5, 8.6 and 8.7 of the Ph. Eur. had been published and were being incorporated into the BP online through in-year updates. Inclusion of the Ph. Eur. General Chapter 5.2.11, Carrier proteins of the production of conjugated polysaccharide vaccines for human use, was noted.

Live Biotheraputic Products Working Party Members were informed that a new Ph Eur Working Party for Live Biotheraputic Products (LBP) had been established and that national authorities had been requested to provide information on the manufacturers.

263 Biological Qualifiers: Update BIO(15)03

Members noted that a system of assignment of Biological Qualifiers to biological substances was continuing to be developed by the WHO.

264 Viral safety of urine derived materials in the pharmacopoeia BIO(15)04

Members were reminded that, at a previous EAG BIO meeting the inconsistencies between the approach taken for viral safety in monographs for urine-derived materials in the BP and EP had been discussed, and that the issue affected the BP specifications for menotrophin and its injection. It had been agreed that any decisions would be deferred until EMA guidelines for the adventitious agent safety of urine-derived medicinal products had been adopted. The guideline had now been adopted and the Secretariat would make proposals for revision of the BP monographs.

265 Vaccine Abbreviations BIO(15)05

Members were informed that a new Ph. Eur. monograph for Influenza Vaccine (Live, Nasal) had been published in supplement 8.5. The abbreviation Flu (Live, Nasal) was proposed for the vaccine. Members agreed that the abbreviation should be included in the BP 2017, subject to confirmation from the Immunological section at the Department of Health.

Additionally the Haemophilus Type b and Meningococcal Group C Conjugate Vaccine monograph had been published in supplement 8.7 replacing the BP vaccine monograph in

April 2016. Members endorsed the proposal that the abbreviation Hib/MenC should be included in the Ph. Eur. monograph.

It was understood that progress was being very slow in the development of a WHO international vaccine abbreviation scheme and further information on the matter was to be sought.

IV NEW MONOGRAPHS

None

V MONOGRAPHS IN PROGRESS

266 Danaparoid Sodium Injection BIO(15)06

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

267 Interferon Alfa-2b Injection BIO(15)07

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

268 Follitropin Injection BIO(15)08

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

269 Desmopressin Nasal Spray BIO(15)09

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

270 Desmopressin Oral Lyophilisate BIO(15)10

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

271 Pancreatin Capsules BIO(15)11

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

VI REVISION OF MONOGRAPHS

272 Heparin Injection: Related substances BIO(15)12

A revised draft monograph for Heparin Injection had been prepared to include the Ph. Eur. test for Related substances present in the monographs for Heparin Sodium and Heparin Calcium. Members recalled that their decision to apply the test to the heparin and LMW heparin product monographs had, in part, been based on the practical results of a survey.

The draft revised monograph had been sent to UK stakeholders and responses received. In view of the stakeholder responses, inclusion of the following statement under the Production statement was proposed and accepted:

'The production method is validated to demonstrate that the product if tested, would comply with the test for Related substances given below'.

Members considered that the statement should also be applied to the low molecular weight heparin injection monographs.

Heparin flush preparations As previously noted 10 and 100 IU/mL preparations, were available for intravenous use where the Ph. Eur. Related substances test was not applicable. The low potency flush preparations were used for the maintenance of patency of intravenous devices by flushing indwelling cannulae and were unlikely to produce blood levels of heparin having any systemic effect. As well as the potency difference between the potency of the flush and injection products, the former products also contained sodium chloride. Members supported a proposal that Heparin flush as a final product should be covered by its own specifications, with clear labelling to avoid its use as an 'antithrombotic'.

273 Dalteparin Injection: Related substances BIO(15)13

As agreed at the previous meeting a draft revised monograph for Dalteparin Sodium Injection had been prepared to include the test for Related substances and sent to the manufacturer for comment. In view of the response, the following statement was agreed for inclusion under the Production statement in the Dalteparin Injection monograph.

'The production method is validated to demonstrate that the product if tested, would comply with the test for Related substances given below'.

274 Enoxaparin Sodium Injection: Related substances BIO(15)14

As agreed at the previous meeting a draft revised monograph for Enoxaparin Sodium Injection had been prepared to include the test for Related substances and sent to the manufacturer for comment. In view of the response, the following statement was agreed for inclusion under the Production statement in the Enoxaparin Injection monograph.

'The production method is validated to demonstrate that the product if tested, would comply with the test for Related substances given below'.

275 Tinzaparin Sodium Injection: Related substances BIO(15)15

As agreed at the previous meeting a draft revised monograph for Tinzaparin Sodium Injection had been prepared to include the test for Related substances and was to be sent to the manufacturer for comment. The following statement was proposed and agreed for inclusion in the monograph.

'The production method is validated to demonstrate that the product if tested, would comply with the test for Related substances given below'.

276 Pancreatin Tablets BIO(15)16

As agreed at the previous meeting (minute 245.1 refers) a draft amendment had been made to the monograph to include a statement under Production concerning dissolution. Members examined the draft and agreed that the statement should be in line with that to be decided for the new monograph for Pancreatin Capsules.

277 Goserelin Implants BIO(15)17

Following a query from a user the Secretariat had reviewed the information supplied by the manufacturer at the time of monograph elaboration. The current requirement for total impurities stated: '*The sum of impurities obtained in tests B and C is not more than 10%'.*

This statement was considered misleading since Test C was a modified version of Test B and had been introduced to ensure the control of impurity 13. The current wording implied that all impurity peaks identified in Test C should be included in the sum of impurities. It was considered that this would result in the duplicate counting of impurities detected by both Tests B and C. Members agreed that, subject to confirmation by the manufacturer, the wording should be revised to: '*The sum of the impurities obtained in test B and impurity 13 in test C is not more than 10%.'.*

VII FUTURE OF BIOLOGICAL MATERIALS IN THE BRITISH PHARMACOPOEIA

278 BIO Strategy Oral BIO(15)18

Members were informed that the BIO Secretariat were currently reviewing the strategy and direction of the BP's BIO work for the next 5 years.

279 MHRA/NIBSC BIO(15)19

Feedback was given on the collaboration between the BP and NIBSC.

280 **Collaboration with other Pharmacopoeias** Oral BIO(15)20

Feedback was given on collaborative activities discussed with other pharmacopoeial authorities.

VIII EUROPEAN PHARMACOPOEIA

281 Comments from the British Pharmacopoeia Commission BIO(15)21

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 26.3, 26.4, 27.1 and 27.2.

282 Comments requested from members on draft texts BIO(15)22

Members were thanked for the comments they had submitted on the monographs published in Pharmeuropa 27.3. They were reminded that comments on draft texts included in Pharmeuropa Volume 27.4 should be submitted by 31 December 2015 either by using the BP Website forum or contacting the Secretariat directly.

283 Texts adopted at the 150th, 151st and 152nd Sessions BIO(15)23

Lists of the documents relevant to the Group that had been adopted at the 150th, 151st and 152nd Sessions of the EPC were provided to members for information.

284 Groups of Experts: Formal Reports BIO(15)24

The most recently available formal reports and summaries of decisions relevant to the work of EAG BIO were noted.

285 Erythropoietin: Request for revision from NIBSC BIO(15)25

A request for revision forwarded from NIBSC was to be considered by the European Pharmacopoeia Commission.

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 5th November 2013 and 6th November 2014
(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 214	**Desmopressin tablets**	**Uniformity of content** The correction to the mobile phase has been included in the BP 2016.
Minute 233	**Bacterial Endotoxin Testing – BP Policy**	At the March meeting, the BP Commission endorsed the additional recommendations from EAG BIO that (1) For new BP Monographs, if the use of a specific method was required, this should be included without a corresponding limit. (2) For existing BP monographs that included a test and limits, no change was necessary.
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 241	**Interferon beta-1a Injection**	This new monograph was published in the BP 2016. Prior to publication a number of changes were made. These changes were agreed with the chair and vice-chair: (1) The limit for oxidised forms was revised from 6 to 9% in-line with the licensed shelf-life limit following comments from a manufacturer. (2) The wording on the choice of method to use for Dimer and related substances of higher molecules was simplified to refer to 'system suitability requirements'. The previous wording was considered to go beyond system suitability and into validation concerns.
Minute 246	**Enoxaparin Sodium Injection**	Changes to the test for Sodium limits were published as agreed in the BP 2016. Investigation into whether additional sample preparation and method details are required in the test are still ongoing. A comment has also been received that the test solution concentration for the test for Light absorption was too concentrated. This is also undergoing checking from the Secretariat.
Minute 247		

List of Acronyms/Synonyms for use by BP Secretariat

Acronym/Synonym	Name
BAN	British Approved Name
BP	British Pharmacopoeia
BP (Vet)	British Pharmacopoeia (Veterinary)
BP Commission	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