BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group: Antibiotics

SUMMARY MINUTES

A meeting of Expert Advisory Group: Antibiotics was held at 151 Buckingham Palace Road, London SW1W 9SZ on Tuesday 27th February 2018.

Present: Dr R Horder *(Chairman),* Dr G Cook (*Vice-chairman*), Mr G Blake, Mr E Flahive, Dr V Jaitely, Dr W Mann, Prof J Miller, Dr M Pires and Mr I Williams. Mr J Sumal attended the meeting for the item discussed under minute 405.

Apologies: None.

In attendance: Mr P Crowley, Mr L Elanganathan, Mr S Maddocks, Ms K Busuttil, Mrs C Galdino and Mr O Ayrton.

382 Introductory remarks

Welcome
The Chair welcomed members to the meeting. A special welcome was extended to Ms Busuttil, Mrs Galdino, and Mr Ayrton from the BP Laboratory.

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.

Freedom of Information
Experts are reminded that any FOI queries that they receive from the media are to be referred to the Secretariat.

Membership
A membership list has been posted on the forum. Members are asked to let the Secretariat know if any of their details have changed.

Professor Derek Calam
Members were informed of the death of professor Derek Calam. Professor Calam had a long involvement with both the British and European Pharmacopoeias. He was a member of the BP Commission for 23 years, including 8 years as Chair (1998-2005). He was involved in the work of a number of BP and EP expert groups over the years including those on Antibiotics, Biologicals and Nomenclature and was a former Chair of the Commission on Human Medicines Expert Advisory Group on Pharmacy and Standards. He was well respected internationally having served as Chair of the WHO International Non-proprietary Names Commission for many years and was a former Chair of the EP Commission.

383 General Matters **ABS(18)01**

Fire evacuation procedure
Members were reminded of the evacuation procedure in the event of a fire alarm.

I MINUTES **ABS(18)02**

384 The minutes of the meeting held on 21st September 2018 were confirmed. It was noted that in minute 376.4 for the Dissolution test of Erythromycin Preparations, the term "coulometric" should be replaced by "colorimetric".

II MATTERS ARISING FROM THE MINUTES ABS(18)03

385 The following matters arising from the meeting held on 21st September 2017 were noted.

Teicoplanin Injection (minute 365.1 refers) The Secretariat were awaiting finalisation of the Ph Eur parent monograph before further developing this monograph.

Lymecycline Capsules (minute 365.2 refers) The test for light absorbing impurities was removed from the monograph in the BP 2016. The Secretariat were awaiting finalisation of the Ph Eur parent monograph before further developing related substances procedure in this monograph.

Liposomal Amphotericin for Infusion (minute 296.2 refers) Although the sole MAH was unwilling to support this monograph, the Secretariat would present proposals for a draft monograph at a future meeting.

Tylosin Premix (minute 365.9 refers) Ph. Eur monograph was updated to include superior related substances method, limits also updated and were tighter.

Azithromycin Preparations (minute 365.12 refers) New monographs for Capsules, Oral Suspension, Powder for Infusion and Tablets were published in the BP 2018. It was agreed that the Secretariat would present proposals for new monographs for Eye Drops and Powder for Oral Solution at a future meeting.

Marbofloxacin Preparations (minute 365.19 refers) These monographs were posted for public consultation with a view to publish in the BP 2019.

Bacterial Endotoxins (minute 365.22 refers) The Secretariat were seeking clarification on the additional information required to remove pyrogens test from remaining Ph. Eur. parent monographs.

Amikacin Injection (minute 366 refers) The suitability of the revised Ph. Eur. procedure was to be assessed. No comments had been received during the public consultation and the drafted assay method was to be published in the BP 2019.

Moxifloxacin Tablets (minute 371 refers) The Secretariat had amended the monograph as discussed and the monograph was posted on the website for public consultation from October to December 2017. No comments were received and the monograph was going to be published in the BP 2019.

Oxytetracycline preparations (minute 372 refers) The Secretariat amended the monographs as discussed and the monographs were posted on the website for public consultation from October to December 2017. No comments were received, and the monographs were going to be published in the BP 2019.

Tobramycin preparations (minute 373 refers) The Secretariat amended the monographs as discussed and the monographs were posted on the website for public consultation from October to December 2017. No comments were received, and the monographs were going to be published in the BP 2019.

Cefoxitin Injection (minute 374 refers) The monograph had been amended and was

going to be published in BP2019, however was not posted on the website as the change was a minor technical change.

Clarithromycin Granules for Oral Suspension (minute 375.2 refers) The Secretariat had confirmed with the laboratory that the resolution requirements for the system suitability can be increased from 1.0 to 1.5 and had revised the monograph accordingly. The Secretariat had revised the solution concentrations and was going to be publishing the monograph in the BP 2019.

Erythromycin Preparations (minute 376 refers) The Secretariat had amended the gradient table in the LC methods. The laboratory requisition had been finalised and the lab had begun the investigation in January 2018. Laboratory work was ongoing.

III MONOGRAPHS FOR THE BP 2019

386 Benzoyl Peroxide And Clindamycin Gel (revised) ABS(18)04

The monograph was first discussed in February 2015 and the sole MAH had expressed that they were willing to support the development of the monograph. The MAH had submitted relevant data and the monograph was originally published in BP 2018.

Identification
It was agreed at the September 2017 meeting that the laboratory would assess the use of dichloromethane in place of chloroform during the Identification procedure. This work was still ongoing and the monograph was going to be revised once the work has been completed.

Related Substances
The related substances procedure had been revised to include the current use of the internal standard according to the manufacturers validation. The concentration of solutions had been revised to mirror the manufacturer's method. Upon consultation and meetings with the MAH technical experts, the drafted monograph was agreed as equivalent.

The method had been successfully verified as part of the establishment of a Clindamycin Phosphate BPCRS.

A Member noted that the limits should be updated to be in-line with the shelf life specification for the sole MAH.

Assay
The Assay was revised to ensure it was in line with the related substances test. The revised method also had approval from the MAH.

Impurities
Following the September meeting, the impurities have had input from both a Member of the EAG, and by EAG NOM and have been finalised in the latest draft of the monograph.

Members endorsed the monograph for publication in the BP2019 following revision of the related substances limits.

387 Colistimethate Preparations ABS(18)05
Colistimethate for Injection (revised)

Colistimethate Powder for Nebuliser Solution (revised)
Colistimethate Inhalation Powder, hard capsule (new)

The Colistimethate for Injection and Colistimethate Powder for Nebuliser Solution monographs were discussed at the September 2017 meeting. Members noted that the Composition specification was wider than that in the drug substance monograph. The Secretariat had discussed the difference with the corresponding manufacturer, and their response and proposals for finalised monographs were presented to members.

The draft monograph for Colistimethate Inhalation Powder, hard capsule, would be included in a future BP publication, subject to comments from manufacturers.

Definition
Members had previously queried whether the definition statement of the Colistimethate For Injection monograph should state “does not contain excipients”. Although this would be true for currently licensed products, the definition had been drafted in line with BP policy to remain open to future formulations. Should a product be developed that did contain excipients, it would be expected to comply with the requirements of the monograph. The Secretariat stated that if any manufacturer found excipient effects interfering with the tests, these would be reviewed at the time to develop alternative methodology.

Members expressed their concerns with this approach as the methods were not validated for any excipient containing products. The Secretariat agreed to raise this issue at a future BP Commission meeting.

Members agreed that the term “aerosols” should be changed to “aerosol” in the Powder for Nebuliser Solution monograph. The Secretariat noted that the current Inhalanda did not include powders for nebulisation, and the monograph would therefore be reviewed once this had been updated.

Composition
The Composition specification proposed at the September 2017 meeting was based on information provided by the manufacturer in their data submission. Members had queried why the limits were wider than those included the parent monograph, which the Secretariat had since discussed with the manufacturer.

The manufacturer had proposed limits based on stability data for the reconstituted product over the course of 24 hours rather than the dry powder. This stability work had been performed by the manufacturer in order to demonstrate that the levels of colistin were maintained within safe limits to support section 6.3 of the Summary of Product Characteristics covering shelf life.

It was noted that the shelf life for reconstituted products is product specific and would be agreed by the MHRA Licensing Division on a case by case basis. BP policy is to control the quality of the product pre-reconstitution, and members agreed that the limits from the Ph. Eur. parent monograph should be retained as the manufacturer had provided shelf life data to demonstrate compliance.

A member noted that the Ph Eur included a limit for the sum of peaks relating to CMS E1 and E2. Members agreed that this limit should be included subject to verification with licensed specifications.

388 **Doxycycline Preparations** **ABS(18)06**
Doxycycline Capsules (revision)

Doxycycline Prolonged-Release Capsules (New)
Doxycycline Tablets (New)
Doxycycline Dispersible Tablets (Revised)

The BP laboratory had carried out the work to assess the Ph. Eur. Related Substances and Assay Doxycycline methods for the revised monographs. The draft monographs were found to be suitable with a couple of minor modifications.

The draft monographs for Doxycycline Prolonged-Release Capsules and Doxycycline Tablets would be included in a future BP publication, subject to comments from manufacturers.

Dissolution
Dissolution tests for the Doxycycline Capsules monograph had been assessed by the laboratory and found to be suitable. The method utilised UV absorbance for the quantification of Doxycycline.

Related Substances
A new isocratic LC method from the Ph. Eur. parent monographs had been harmonised across the Doxycycline monographs, and its suitability investigated by the BP laboratory. The method was found to be suitable for all available products across the different preparations.

The method had been drafted into the revised monographs. The limits that were specified in the latest draft of the Ph Eur Parent monograph had been adopted, with the exception of the unspecified impurity limit which was increased in-line with ICH Q3B (R2). Members noted the limits were tighter than some licensed specifications, but they were agreed in the absence of any comments at public consultation.

Assay
The Assay method was harmonised with the related substances method. The draft assay method for was investigated by the laboratory and found to be suitable for all samples tested, with minor modifications.

Two separate batches of capsules produced lower than average results, however were still within specification. The Secretariat had contacted the manufacturers specifically to make them aware of the monograph that is available during the public consultation window from January to March.

The members endorsed the draft monographs for publication in the BP2019 pending editorial amendments suggested.

389 **Doxorubicin Preparations** **ABS(18)07**
Doxorubicin Sterile Concentrate (Revised)
Doxorubicin for Infusion (Revised)

Issues had been raised by manufacturers since the replacement of the Doxorubicin Injection monograph and Doxorubicin for Injection sub monograph with the Sterile Doxorubicin Concentrate and Doxorubicin for Infusion monographs in the BP 2018. These were presented to members with a view to publishing the revised monographs in the BP 2019 along with a notice of intent to revise.

Title
The Doxorubicin Injection monograph had been proposed for revision at the February 2016 meeting in order to separate the Solution for Injection from the Powder for

Solution for Injection monographs due to confusion between different content limits for each product.

EAG PCY advice had been sought on the naming of these monographs. It had been agreed that the solution monograph should be named Doxorubicin Sterile Concentrate in line with how the products were administered, and that the monograph for powders should be named Doxorubicin for Infusion or Injection as both methods of administration was common. The publication of the revised monographs in the BP 2018 had been agreed at the September 2016 meeting, following a public consultation between October and December 2016 through which no comments were received.

A request had then been received from a manufacturer to harmonise impurity limits with the USP, and the monographs were reviewed at the September 2017 meeting. It was also highlighted that a number of different pharmaceutical forms as solutions existed, and members agreed that subsidiary titles of Doxorubicin Infusion and Doxorubicin Injection should be added to the Sterile Doxorubicin Concentrate monograph in the BP 2019, given the similarity of the solution formulations.

Following the release of the BP 2018, a MAH had contacted the Secretariat noting that the monograph for Doxorubicin Injection had been omitted. They expressed a concern that there was no longer a public standard for their licensed solution for injection product.

The Secretariat had reviewed the SPCs of all marketed products and noted that all ready to use solution products contained the same excipients, as did all the powder based products. All SPCs stated that the products could be administered via a freely running intravenous infusion and most stated intravesical bladder instillation. Administration by direct or bolus injection was noted in some SPCs for concentrates, powders for solution for injection and solution for injection, but all state that this is not a recommended route due to an increased risk of adverse events.

A member had consulted colleagues who noted that the Doxorubicin for Infusion monograph title should state Infusion/Injection based on its use. The Secretariat indicated that the current title for its primary use was in-line with BP policy. The subsidiary title of “Doxorubicin for Injection” indicated its secondary use. It was also noted that the products were used for bladder irrigation, but members agreed that this did not require a separate monograph as the product labels only specified this as an additional use.

Members agreed that a single monograph called “Doxorubicin Sterile Concentrate” should be developed, with “Doxorubicin for Injection” and “Doxorubicin For Infusion” as subsidiary titles.

The Secretariat agreed to investigate additional wording in the definition to indicate the multiple administration routes.

Content
In line with the decision to develop a single monograph, members agreed that the limit should be widened to 92.5 – 110.0 %.

390 **Moxidectin Preparations** **ABS(18)08**
Moxidectin Injection (Revised)
Moxidectin Oral Solution (Revised)
Moxidectin Oromucosal Gel (Revised)

At the EAG meeting in September 2016, the draft monographs for Moxidectin Oromucosal Gel, Moxidectin Oral Solution and Moxidectin Injection were presented to the group after the adoption of methods drafted from the sole MAH. The monographs were approved for publication in the BP2018 following public consultation, for which no responses were received.

Following comments from VMD regarding limits in the related substances test, the monographs were reviewed.

Related Substances
The Secretariat had revised the related substances procedures in the Oromucosal Gel and Oral Solution monographs to harmonise with the Injection monograph.

Limits
The Secretariat had made changes to the limit for "the sum of all secondary peaks" from 2% up to 7% after a request from the VMD to bring in line with current licensed specifications.

The changes were accepted by the members and monographs approved for publication in the BP2019.

391 Norfloxacin Tablets (Revised) ABS(18)09

During a Laboratory re-test of the Norfloxacin BPCRS, it had been found that the concentrations of solutions used in the TLC Identification test were inappropriate due to streaking of the spots.

Identification
The reduction of application volume from 50 µL to 5 µL resulted in improved chromatographic separation, and members agreed that the monograph should be amended to reflect the Laboratory findings.

A member proposed that chloroform was replaced by dichloromethane in the mobile phase as it was used as a diluent and the Secretariat agreed to amend the monograph.

Related substances
Members requested that the Secretariat should investigate the inclusion of a Related substances test based on the Ph. Eur. Related substances test. The Secretariat noted that it would be added to the work programme.

392 Tigecycline For Infusion (New) ABS(18)10

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

MONOGRAPHS FOR THE BP 2020

393 Benzylpenicillin Injection (Revised) ABS(18)11

A revision to the Benzylpenicillin Sodium and Benzylpenicillin Potassium Ph. Eur. monographs had been published in Ph. Eur. supplement 9.2, which included an improved HPLC method for Related substances and Assay. The Secretariat had prepared a revised monograph for the Benzylpenicillin Injection monograph in light of these changes.

Title
The Secretariat noted that all marketed products were powders for solution for injection or infusion. Members agreed to change the monograph title to Benzylpenicillin for Injection, with a subsidiary title of Benzylpenicillin for Infusion.

Definition
The drafted definition stated that "… is a sterile material consisting of Benzylpenicillin Potassium or Benzylpenicillin Sodium with or without excipients", and members questioned this as all marketed products did not have excipients. The methods were not validated for products without excipients, and it was thought to be unlikely that manufacturers would add excipients.

Identification
There were three identification tests included in the published monograph. An infrared test had been included based on the assumption that the formulated preparation would produce a concordant spectrum to the API refence material, as the products had no excipients. Members agreed that a laboratory evaluation was not required as the licensed products did not contain excipients.

Related substances
The Ph. Eur. had published a new Related substances method which identified impurities A through to H. The new method utilised a gradient program with a run time of 22 minutes (without re-equilibration), whereas the current Related substances test in the published Benzylpenicillin Injection monograph had a gradient program lasting for 50 minutes (with re-equilibration).

The new test controlled impurities A through to H, and had caused the BP limits to be tighter than the Ph. Eur. in the case of impurity E. The impurity limits for the current Ph. Eur., BP, and MAH specifications were compared along with the proposed BP limits.

Members agreed that laboratory evaluation was not required given the licensed products did not contain excipients.

It was noted that the MAHs controlled impurity F at a tighter limit than the Ph. Eur. limit, but members agreed that the BP monograph should be in line with the Ph. Eur. monograph.

It was also suggested that the monograph could have separate limits for each salt, and that the MAHs should be contacted to confirm suitability of limits.

Assay
Members agreed to the procedure containing chromatographic conditions harmonised with the related substances as for the Ph Eur Assay procedure.

394 Phenoxymethylpenicillin Preparations ABS(18)12
Phenoxymethylpenicillin Oral Solution (Revised)
Phenoxymethylpenicillin Tablets (Revised)

A revision to the Phenoxymethylpenicillin Potassium Ph. Eur. monograph had been published, which included an improved HPLC method for Related substances and Assay. The Secretariat had drafted revised monographs for the Phenoxymethylpenicillin Oral Solution and Tablets monograph in light of these changes.

Definition (Oral Solution)
The Secretariat noted that all licensed products were powders/granules for solutions

and that the published monograph instructed the user to reconstitute the product. Members requested that the Secretariat reviewed the consistency of oral solution/suspension preparation monographs and this issue be raised with the BP Commission. A member noted that specifications for the dry product and the reconstituted product were required for Licensing.

Content
The content was stated as the sum of phenoxymethylpenicillin and 4-hydroxyphenoxymethylpenicillin (impurity D), but the current BP monographs did not provide a method of quantifying this active impurity. As the Related substances chromatographic conditions had been employed for this test too, it had been incorporated into the Related substances test.

Related substances
The Ph. Eur. had updated the Related substances method which allowed for greater control of impurities. Both of the published product monographs did not contain a related substances test.

A method evaluation had been carried out to assess the risk of using the Ph. Eur. method for the licensed products. Members agreed that laboratory evaluation should be carried out as the marketed products had varying formulations.

Members noted that although the Ph Eur controlled Impurity D through a separate test which used the related substances procedure with a specific limit but agreed that Impurity D should be controlled as part of the Related substances test.

Members also requested that the wording of the limit statement for impurities E and F should be amended to reflect that they are epimers/isomers.

Assay
The chromatographic conditions were harmonised with the related substances for analytical convenience. Members noted that the content should be calculated as the sum of phenoxymethylpenicillin and 4-hydroxymethylpenicillin in line with the Ph Eur.

Members agreed that the BP laboratory should assess the suitability of the drafted procedures for licensed products.

395 **Clindamycin Preparations** **ABS(18)13**
Clindamycin Veterinary Tablets (New)
Clindamycin Capsules (Revised)
Clindamycin Injection (Revised)
Clindamycin Gel (New)
Clindamycin Vaginal Cream (New)
Clindamycin Lotion (New)
Clindamycin Cutaneous Solution (New)

The draft monographs for Clindamycin Veterinary Tablets, Gel, Vaginal Cream, Cutaneous Emulsion and Cutaneous Solution would be included in a future BP publication, subject to comments from manufacturers

Dissolution
The Secretariat had drafted a revision to the Clindamycin Capsules monograph containing a harmonised USP dissolution test.

A member suggested that the quantification method be harmonised with the related

substances method. The secretariat believed that the drafted quantification method was preferred due to the decreased run time.

Related Substances
The LC procedure from the published clindamycin phosphate Ph. Eur. monograph had been drafted for the Clindamycin Injection monograph which applied gradient conditions and quantification at 210 nm. This method was an improvement on the original related substances procedure as it contained better control over related substances.

The impurity limits had been drafted based on a review of other compendial monograph limits and MAH specifications.

Members agreed that the BP Laboratory should assess the suitability of the procedure and limits for licensed products.

Assay
The LC procedure from the published clindamycin phosphate monograph was drafted for all Phosphate product monographs which applied gradient conditions and quantification at 210 nm. The draft method was harmonised with the Related Substances procedure. Given the complex nature of the products, the sample extraction for the test solutions was based on the USP Clindamycin Vaginal Cream monograph.

Members agreed that the BP laboratory should investigate an isocratic method for the Assay and assess its suitability for licensed products.

396 Minocycline Preparations **ABS(18)14**
Minocycline Tablets (Revised)
Minocycline Capsules (New)
Minocycline Prolonged-Release Capsules (Revised)

The BP laboratory had carried out work to assess the suitability of the Ph. Eur. Related Substances and Assay methods, along with the draft infrared identification. The draft revised monographs were all found to be suitable with a couple of minor modifications.

The draft monographs for Minocycline Capsules would be included in a future BP publication, subject to comments from manufacturers.

Identification
The IR identification methods for the Minocycline prolonged-release capsules and Minocycline Tablets monographs were investigated by the laboratory. The extraction and drying procedure had been adjusted by the laboratory to give concordant and reproducible spectra. A modification had been made to the monographs to reflect the change.

Related Substances
A new isocratic LC method from the Ph. Eur. parent monograph had been harmonised across the monographs. The methods were found to be suitable for all available products tested, across the different preparations.

There were a few occasions where the limits for both Impurity A and “any other secondary peak” were found not to be suitable.

The drafted limits for Impurity A had been increased from 1.2% to 2.0% in line with majority of the currently approved specifications. The Secretariat noted that some of the older specifications stated 3.0% but this was based on previous BP/Ph. Eur.

methodology. All products tested by the laboratory easily complied with the drafted limits of 2.0%. The limits for any other impurity had been increased from 0.2% to 0.3%, these limits were tighter than those that could be seen in the majority of specifications, however those specifications were based on old methodology. All products tested by the BP laboratory would comply with this new specification.

The identity of one of the unspecified impurities was unknown, this impurity was found to be consistently at ~0.20-0.25% in a number of the products tested by the laboratory. It was discussed that the limit for any other impurity should be kept at 0.2% for the public consultation. This process was approved; however, it was made clear that all manufacturers should be contacted specifically when the monographs were placed on the website.

Assay
The Assay method was harmonised with the related substances method for the draft revised monographs and was investigated by the laboratory who found to be suitable for the majority of samples tested.

The extraction procedure for the Prolonged-Release Capsules was changed to whole capsules and the diluent was changed to include an organic component, it was found that this aided the dissolution of the gastro-resistant coating on the second “tablet” within the capsule and therefore allowed full extraction of the Minocycline. The monograph had been updated to reflect the change.

The members confirmed the suitability of the methods for inclusion in the respective draft monographs.

MONOGRAPHS FOR BP2021+

397 Caspofungin For Injection (New) ABS(18)15

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

398 Ciclosporin Preparations ABS(18)16
Ciclosporin Eye Drops (Revised)
Ciclosporin Eye Ointment (VET, New)

The elaboration of a revised monograph for Ciclosporin Eye Drops was discussed. It was noted that the Ph. Eur. were assessing the suitability of a revised Related substances method, which included revised limits and an additional impurity. The Secretariat would track the progress of this and Members agreed that progression of these monographs should be held until the Ph Eur assessment was complete.

A monograph for Ciclosporin Eye Ointment would be included in a future BP publication, subject to comments from manufacturers.

Eye Drops
The Secretariat noted that a license had been granted by the EMA for the previously unlicensed eye drops. The published ULM monograph did not contain a Related substances test. A laboratory investigation (LR 5571) had been carried out, and a common Related substances and Assay test in line with the Ph. Eur. parent monograph were found to be suitable. However, the revised monograph hadn’t been progressed as the Secretariat were waiting on comments from the manufacturer regarding the limits.

It was noted that the unlicensed product had a very different formulation to the licensed product, and therefore members endorsed a laboratory evaluation to be carried out.

399 **Ciprofloxacin Preparations** **ABS(18)17**
Ciprofloxacin Ear Drops (New)
Ciprofloxacin Eye Drops (Revised)
Ciprofloxacin Eye Ointment (New)
Ciprofloxacin Infusion (Revised)
Ciprofloxacin Oral Suspension (New)
Ciprofloxacin Tablets (Revised)

The draft monographs for the Ciprofloxacin Ear Drops, Eye Ointment and Oral Suspension would be included in a future BP publication, subject to comments from manufacturers.

Title
3 forms of Ciprofloxacin were used in the Ciprofloxacin Infusion products, and the title applied to all forms as written. The Ciprofloxacin Eye Drops monograph was intended to apply for the licensed Ciprofloxacin Hydrochloride products as well as the unlicensed Ciprofloxacin Lactate product. The Secretariat noted that all other products contained a single form, so the salt was not required.

Definition
Standard definitions in line with BP policy had been drafted for the majority of products based on the single API form being used.

As multiple forms were used for the infusion, a definition covering all of these had been drafted. The preparation of ciprofloxacin hydrogen sulphate is described as “by the interaction of Ciprofloxacin and Sulfuric Acid”. The preparation of ciprofloxacin lactate remained as described.

The definition for Ciprofloxacin Eye Drops has been updated to cover both the licensed and unlicensed product.

Identification
Members recommended that a suitable IR method is investigated by the BP Laboratory.

Acidity or Alkalinity (Infusion only)
Members agreed for the previously published limits to be retained in the monograph, in line with the licensed specifications.

Related Substances
The related substances procedure of the monographs being revised had been editorially updated in line with current policy.

Limits had been drafted based on the Ph. Eur. limits for the drug substances used, with a view to accommodate specifications of the licensed products. Base limits for unspecified and disregard had been drafted in-line with ICH Q3B(R2).

Members were informed that limits for the previously published Eye Drops, Infusion and Tablets monographs had been tightened where the specifications allowed, and the disregard increased in line with ICH Q3B(R2).

Members agreed that a review of limits against the licensed specifications should be undertaken.

400 **Co-Amoxiclav Preparations** **ABS(18)18**
Co-Amoxiclav Injection (Revision)
Co-Amoxiclav Oral Suspension (Revision)
Co-Amoxiclav Tablets (Revision)
Co-Amoxiclav Dispersible Tablets (Revision)

The Ph. Eur. monographs for Amoxicillin Sodium and Amoxicillin Trihydrate were nearing publication of a revision to the related substances procedure. The procedure was viewed as superior to the published related substances procedure. This superior method facilitated a review of the limits for impurities of Amoxicillin controlled by the monographs.

The Secretariat had performed a full monograph review for the Co-amoxiclav product monographs for the Injection, Oral Suspension, Tablets and Dispersible Tablets preparations and had prepared revised draft monographs for each preparation. The Secretariat proposed that the laboratory assess the revised related substances procedure in the drafted monographs.

It was noted by the Secretariat that the definition statement referencing Co-amoxiclav liquid preparations was omitted from the Co-amoxiclav Injection monograph as there were no licensed co-amoxiclav Injection products on the market that were produced as liquids.

Title
A new policy on the naming of monographs had been approved by Commission, stating that monograph titles should be bought in-line with standard terms. Therefore, the title of the Dispersible Co-amoxiclav Tablets was amended to “Co-amoxiclav Dispersible Tablets”.

Related Substances
The related substances procedure for the Amoxicillin component of each product had been drafted using the new Ph. Eur. method. The extraction methods for the various preparations had been drafted using existing procedures, substituting the diluent for the Ph. Eur. revised diluent. Limits for impurities had been revised in line with the Ph Eur and current MAH specifications.

Members agreed that laboratory work should be undertaken by the BP laboratory in order to assess the suitability of the methods in the draft monographs for licensed products on the market. It was noted that any requisition should also include Amoxicillin monographs and products.

Assay
The published Assay procedure quantified both actives and members agreed that this should be retained rather than harmonise with the new Ph Eur procedure.

401 **Enrofloxacin Preparations** **ABS(18)19**
Enrofloxacin Tablets (New)
Enrofloxacin Oral Solution (New)
Enrofloxacin for Injection (New)

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

402 **Rifampicin preparations** **ABS(18)20**
Rifampicin Capsules (Revision)

Rifampicin for Infusion (New)
Rifampicin Oral Suspension (Revision)

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

Related Substances
It was noted that the existing impurity limit for 3-formylrifamycin was below the innovator's shelf-life specification limit for the Capsules monograph and members agreed that it should be increased to reflect what was licensed.

Assay
The Assay procedure had been updated from a non-specific test by UV absorption to a specific LC method with quantification at 254 nm that had been adopted by the International Pharmacopoeia.

Members agreed that the BP Laboratory should assess the suitability of the draft procedures.

403 Rifampicin Combination Preparations ABS(18)21
Rifampicin and Isoniazid Tablets (New)
Rifampicin, Isoniazid and Pyrazinamide Tablets (New)

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

404 Semi-synthetic Antibiotics ABS(18)22

A paper was presented by Mr Flahive seeking input from members surrounding the classification of semi-synthetic antibiotics. Members agreed that semi-synthetic antibiotics were not biologics and have not been historically treated so.

It was proposed that Mr Flahive should request the issue be raised through trade associations to QWP to confirm the situation surrounding this class of medicines.

405 Use Of Fish Peptone In Manufacture Of Antibiotics ABS(18)23

Mr Sumal introduced a short presentation regarding an ongoing issue with the use of fish peptones in the fermentation process of the manufacture of certain antibiotics.

406 Antimicrobial Resistance ABS(18)24

Due to time constraints, discussion of this item was deferred to a future meeting.

407 Review Of The Use Of Antimicrobial Assays ABS(18)25

The Secretariat noted that that the Ph Eur remove the microbiological conditions for specific drug substance Assays from the microbial assay of antibiotics, Appendix XIV A, when an Assay in the drug substance monograph is updated to a physico-chemical test. This caused issues for BP drug product monographs which relied on this information.

It was proposed that the Secretariat should include the required Assay conditions in the appendices as soon as possible.

Post meeting Secretariat note: *This action had already been taken and is visible in the*

Hardcopy version of the publication. However, the text did not appear on the website. This is an issue that can be fixed and will be uploaded for the Ph. Eur. 9.5 supplement update.

Due to time constraints, the remainder of this item was deferred to a future meeting

408 2018 BP Membership Review ABS(18)26

Members were informed that a membership review for all BP Expert Advisory Groups that was happening at the end of the year. The process to be used was presented for information and members would be requested to confirm their ongoing membership at a later date.

409 Work Programme ABS(18)27

The current work programme for ABS was provided for the members information.

Members endorsed the revision of the Amoxicillin monographs and the addition of Clindamycin Lotion to the work programme. Members endorsed the omission of Clindamycin Oral Powder from the work programme due to the absence of data supporting use in the UK.

A summary of updates to Ph Eur antibiotic monographs and potential affects to BP monographs as well as the BP laboratory work plan were presented for information.

410 British Pharmacopoeia Matters ABS(18)28

A summary of the minutes from the latest BPC meeting was presented for information.

411 European Pharmacopoeia ABS(18)29

The minutes and informal report from the group 7 meeting was presented for information.

Monographs on Pharmeuropa were highlighted and the deadline for comments noted by Members.

412 Any Other Business

None.

413 Date of Next Meeting

The date of the next meeting is the 27th September 2018. It was noted that this meeting will be held at the Agency's new headquarters in Canary wharf.