BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group (EAG): Herbal and Complementary Medicines (HCM)

SUMMARY MINUTES

A meeting of this Expert Advisory Group was held at 151 Buckingham Palace Road, London, SW1W 9SZ on 21st June 2016.

Present: Prof E Williamson (*Chair*), Dr L Anderson (*Vice-Chair*), Mr P Anderson, Dr K Helliwell, Dr R Middleton, Mr B Moore, Dr M Pires, Dr M Rowan, Prof M Simmonds, Dr K Strohfeldt-Venables, Mr C Welham and Dr K Zhao.

Apologies for absence: Prof A Bligh, Ms C Leon, Mr J Sumal
Prof S Gibbons did not attend the meeting.

In attendance: Dr P Holland, Dr R A Pask-Hughes, Mr M Whaley
Dr C Howard, Ms C Lockie-Williams, Ms C Gkouva, Mr L Gibson
Mr D Holcombe, Ms F Lee.

514 **Introductory Remarks**

Welcome The Chair welcomed members and extended a particular welcome to staff from both the BP Laboratory and the BP-NIBSC Herbal Laboratory.

Comments had been received from a corresponding member and these were taken into consideration during the discussions and decisions of the relevant agenda items.

Declaration of Interests Participants were asked to declare any interest they might have, where appropriate, before the start of the discussion of each paper.

I MINUTES

515 The minutes of the meeting held on 25 November 2015 were confirmed.

II MATTERS ARISING FROM THE MINUTES

516 A list of matters arising from the minutes of the meeting of EAG HCM held in November 2015 and on-going matters arising from previous meetings was provided. A copy is appended.

Minute 487 Phyllanthus Amarus With receipt of the BP-NIBSC Herbal Laboratory analyses and authentication, the work on the monograph would be continued. The received information relating to Identification tests A and B would be included in the revised draft monograph.

Minute 509 Liquorice Liquid Extract A full report on the reformulation should be available at the November 2016 EAG meeting.

III REPORTS AND CORRESPONDENCE

517 Transfer of Herbs to EDQM HCM (16)1

As agreed by EAG HCM and endorsed by the BP Commission, the Secretary to the UKD had requested that the 9 herbs in a multicomponent product that were not covered by Pharmacopoeial specifications, should be added to the EDQM work programme.
It was noted that products containing neem (*Azadirachta indica*) fruit were not permitted to be marketed in Australia. Neem fruit for human internal use came within the category of '*Substances of such danger to health as to warrant prohibition of sale, supply and use*'.

518 BP 2017 HCM Monographs and Texts HCM (16)2

A list of new and revised texts included for publication in the BP 2017 was received. This included the new BP monograph for Vitex Negundo Leaf and the new BP Supplementary chapter VII D: DNA Barcoding as a Tool for Botanical Identification of Herbal Drugs in addition to 9 new Ph. Eur. monographs for certain herbal drugs and materials for use in the manufacture of homoeopathic preparations. Two BP monographs had been revised: Berberis Aristata (Identification test C; D-Tetrahydropalmitine; Assay) and Gastro-resistant Peppermint Oil Capsules (Composition of peppermint oil). The monograph for Liquorice Liquid Extract was being omitted by means of the BP 2017. The monograph for Cinnamon Tincture had been suppressed by the European Pharmacopoeia Commission as from 1st of April 2016.

Supplementary chapter VII D Two editorial amendments had been agreed at the June 2016 meeting of Panel DNA: Identification Techniques**.** One amendment concerned the definition of Sanger sequencing that was changed to 'The method by which a DNA sequence is resolved, developed by Frederick Sanger and colleagues'. It had also been noted that 'Sanger' could be replaced by 'dye terminator sequencing'. The amendment was also to be applied to the glossary in the BP 2016 Appendix XI V 'Deoxyribonucleic Acid (DNA) Based Identification Techniques for Herbal Drugs.'
The second amendment was to Table 2: under Criteria for acceptance: the text 'Lane 2' appeared twice.
It was commented that inclusion of the sequences on the database Genbank would assist validation of the dataset.

519 Pyrrolizidine Alkaloid Contamination HCM (16)3

The EAG noted the recall of some batches of a St John's Wort THR product by the MHRA. Because Pyrrolizidine alkaloids (PAs) were not found in St. John's Wort itself, the contamination had been likely caused by accidental collection of local weeds during harvesting.

The EAG also noted controls being introduced to address contamination of herbal medicinal products with toxic, unsaturated pyrrolizidine alkaloids (PAs). The public statement on contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids can be found on the EMA website (http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2016/06/WC500208195.pdf).

520 Aristolochic Acids in Herbal Drugs HCM (16)4

The Chair of the BP Commission had received a copy of a paper from the Journal of Natural Products on "LC-MS- and 1H NMR-Based Metabolomic Analysis and *in Vitro* Toxicological Assessment of 43 Aristolochia Species.". The paper had been co-authored by

3 groups including 2 UK institutions. The paper detailing a more comprehensive method to detect more compounds which were believed to cause aristolochic acid nephropathy was presented for consideration. The Secretariat highlighted that the current Ph. Eur. methods would not detect all aristolochic acid analogues which the paper suggested contributed to aristolochic acid nephropathy. It was explained that the aim of the methodology currently included in the Ph. Eur. had been to detect aristolochic acid I and aristolochic acid II.

The group discussed the paper and agreed that the findings of the research were important to note. It was noted that due to the UK banning order on aristolochic acid containing herbal drugs and 'confusables' the situation in the UK was different to the situation in other Member States. The group endorsed the actions of the Secretariat who had provided the paper to the EDQM for consideration.

IV MONOGRAPHS IN PROGRESS

521 **Clivers (Cleavers)** HCM (16)5

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

522 **Spearmint** HCM (16)6

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

523 **Nutmeg** HCM (16)7

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

524 **Sandalwood Oil** HCM (16)8

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

525 **Tribulus Terrestris Fruit** HCM (16)9

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

V NEW MONOGRAPHS

526 **Capsicum Oleoresin; Capiscum Tincture** HCM (16)10

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

527 **Calcium Sennosides** HCM (16)11

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

528 **Glehnia Littoralis Root** HCM (16)12

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

VI REVISION OF MONOGRAPHS

529 Gastro-Resistant Peppermint Oil Capsules HCM (16)13

Members recalled that it had been realised that the limits given in the monograph for Gastro-Resistant Peppermint Oil Capsules had been based on those in the Ph. Eur. method in the oil monograph prior to revision of the oil monograph limits. The Secretariat had contacted the manufacturers concerning revision of the limits to those in the current Ph. Eur. monograph. A response had been received from one manufacturer confirming acceptance of the proposed revision. The revision had been included in material for the BP 2017. Comments had been received from members of the BP Commission on the DRT draft text, the outcomes were as follows.

Definition Since 'Enteric capsules' was not a Standard Term it had been advised that the term was deleted and to instead to include 'They are covered with a gastro-resistant coating'. This had been undertaken.

Identification A It was confirmed that the text was the same as that in the Ph. Eur. monograph for Peppermint Leaf and so no change was made. A comment had also been made on the length of the description of the developed zones. Consequently the Secretariat would consider inclusion of a diagram of the developed plate.

Tests: Disintegration A comment had been made suggesting inclusion of a time of operation of the apparatus, such as 2 hours. It was accepted that the key with the dissolution was to ensure no release of peppermint oil into the stomach and therefore a long lag time was needed. Consequently no amendment to the text was made.

Composition of peppermint oil The Secretariat will confirm whether the ratio of cineole to limonene should be expressed as ‘greater than 2’ rather than ‘not less than 2’. The need to include a ‘limit of disregard’ will also be checked by the Secretariat at the earliest opportunity.

530 Peppermint Products HCM (16)14

Peppermint Spirit Since the current monograph had no test for identification and there were no chromatographic profile limits on the oil components, the Secretariat had tried to identify stakeholders concerning possible application of the chromatographic profile test as specified in the *Ph. Eur.* monograph for Peppermint Oil, but none had been found. There was no licensed product. Members agreed that, rather than revise the monograph to include the chromatographic test and then omit from the BP with the best possible specifications, the monograph should be omitted from the next publication.

Concentrated Peppermint Emulsion The BP monograph had been omitted from the BP 2016 as agreed since it did not include any identification, tests or oil analysis. The Secretariat had made enquiries concerning the composition of the product and applicability of the chromatographic profile test. Two stakeholders had been identified and would be contacted for further information. It was commented that the 2% oil was recoverable from the formulation.

Peppermint Oral Solution Members noted that the monograph was ‘on hold’ until such time that the active ingredient could be assayed with acceptable precision and other analytical issues addressed.

Peppermint Oil Enema Information had been received that the formulation, containing Peppermint Oil (0.8%), polysorbate and water, was produced and used within the NHS.

The Secretariat would make further enquiries concerning the actual products and degree of use.

VI EUROPEAN PHARMACOPOEIA

530 **European Pharmacopoeia Reports** HCM (16)15

Informal reports for EDQM Groups of experts and a Working Party were discussed.

VII ANY OTHER BUSINESS

531 Members were asked for their views on storing herbal drugs with silica gel as a means of preservation and its impact on the water content of the herbal drug and the loss on drying data generated by the BP Laboratory.

It was confirmed that other institutions stored herbal samples using silica gel (in conjunction with storage at 15°C). It was accepted that the impact of such storage methods on the analytical data generated should be insignificant if the silica gel is stored outside of the drugs primary packaging.

513 **Programme of Meetings**

2016
Wednesday, 23rd November

2017
Thursday, 22nd of June
Thursday, 23rd of November

MATTERS ARISING FROM PREVIOUS MEETINGS OTHER THAN THOSE MENTIONED ON THE AGENDA

Meeting June 2016

Note from the Secretariat

Minute 335 Chrysanthemum Flower
To be progressed at the earliest opportunity.

Minute 357 Spearmint Oil
The action concerning revision of the oil monograph would be addressed at the earliest opportunity.

Minute 358 Adhatoda Vasica Root (Malabar Nut)
The EDQM are in the process of elaborating a monograph for Adhatoda Vasica Leaf. In view of this work the BP monograph for Adhatoda Vasica Root to be re-started at a point when the Ph Eur monograph is further progressed.

Minute 359 Cyperus Rotundus
To be progressed at the earliest opportunity.

Minute 405 Opium Tincture
Revision of the monograph would be investigated at the appropriate time.

Minute 446 Dill Oil
Some samples have been received and work on the assessment of a test for apiole will be considered at the earliest opportunity.

Minute 460 Standardised Senna Leaf Dry Extract
No further data was received to support a request for the revision to the test for loss on drying. The action will be considered completed.

Minute 487 Phyllanthus Amarus
Work on the authentication of the samples of *Phyllanthus amarus* has recently been completed by the BP-NIBSC Herbal Laboratory. The HPTLC work will be reviewed using the available authentication data. Monograph elaboration will recommence and a paper will be presented at the earliest opportunity.

Minute 497 Sample Procurement
The form concerning sample procurement has been amended.

List of Acronyms/Synonyms

Acronym/Synonym	Name
APhI	Ayurvedic Pharmacopoeia of India
ARTG	Australian Register of Therapeutic Goods
ATA	Ayurvedic Trade Association
BHP	British Herbal Pharmacopoeia
BHomP	British Homoeopathic Pharmacopoeia
BP	British Pharmacopoeia
BP (Vet)	British Pharmacopoeia (Veterinary)
BP Commission	British Pharmacopoeia Commission
BPCx	British Pharmaceutical Codex
BPCRS	British Pharmacopoeia Chemical Reference Substance
BS	British Standard
CMPACC	Chinese Medicinal Plants Authentication and Conservation Centre (Kew)
CEP	Certification Procedure for the European Directorate for the Quality of Medicines
CHM	Commission on Human Medicines
CP	Pharmacopoeia of the People's Republic of China
CRS	Chemical Reference Substance
EAG	Expert Advisory Group
EPC	European Pharmacopoeia Commission
EPCRS	European Pharmacopoeia Chemical Reference Substance
EU	European Union
FDA	Food and Drug Administration
FIP	International Pharmaceutical Federation
FoI	Freedom of Information
GC	Gas chromatography
GMP	Good Manufacturing Practice
HAB	German Homoeopathic Pharmacopoeia
HKCMMS	Hong Kong Chinese Materia Medica Standards
HMPC	Herbal Medicinal Products Committee
ICH	International Conference on Harmonisation
IR	Infrared
ISO	International Organisation for Standardisation
JP	Japanese Pharmacopoeia
LC	Liquid chromatography

LD	Licensing Division
LGC	Laboratory of the Government Chemist, Teddington
LR	BP Laboratory Report
MAIL	Medicines Act Information Leaflet
MHRA	Medicines and Healthcare products Regulatory Agency
MPNS	Medicinal Plant Names Services - Royal Botanic Gardens, Kew
NIBSC	National Institute for Biological Standards and Control
NPA	National Pharmacopoeial Authority
OMCL	Official Medicines Control Laboratory
Ph Eur	European Pharmacopoeia
PMU	Pharmacy Medicines Unit – to be confirmed
QSIMP	Quality Standards of Indian Medicinal Plants
SPC	Special Product Characteristics
TGA	Therapeutic Goods Administration, Australia
THMPD	Traditional Herbal Medicinal Products Directive
TLC	Thin layer chromatography
UK	United Kingdom
UKD	United Kingdom Delegation [to the European Pharmacopoeia]
USP	United States Pharmacopeia
UV	Ultraviolet
WHO	World Health Organization