31 July 2018
EMA/CHMP/523753/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

ORGAM[1] minutes of the meeting on 16 July 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review.

Of note, the minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

[1] The CHMP ORGAM is a meeting to discuss CHMP organisational matters. It is a virtual meeting, which usually takes place on Monday before the CHMP Plenary meeting. CHMP members, working party chairs and national experts together with EMA staff are participating in this forum. Depending on the nature of the issue and availability of documents and experts some ORGAM topics can be discussed at the CHMP Plenary. Please note that the ORGAM meeting is not taking place every month.

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1.1. Welcome and declarations of interest of members, alternates and experts

1.2. Adoption of agenda

CHMP ORGAM agenda for 16 July 2018 meeting

1.3. Adoption of the minutes

CHMP Orgam Minutes of July 2018 meeting will be adopted at the July 2018 CHMP plenary.

2. Working Parties, Committees, SAGs and Drafting Groups

2.1. General

2.1.1. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Call for nomination of a new SWP chairperson following the end of mandate of Jan Willem van der Laan in October 2018.

Nominations should be sent by **12th October 2018**

Interested candidates should send a cover letter and CV to the CHMP secretariat ahead of the deadline.

Action: For information

The CHMP noted the call.

Final minutes for SWP meeting held by teleconference on 20 March 2018 (EMA/CHMP/SWP/180320/2018)

Action: For information

The CHMP noted the minutes.

Final minutes for SWP meeting held by teleconference on 24 April 2018 (EMA/CHMP/SWP/265928/2018)

Action: For information

The CHMP noted the minutes.

Final minutes for SWP meeting held by teleconference on 29 May 2018 (EMA/CHMP/SWP/366427/2018)

Action: For information

The CHMP noted the minutes.

2.1.2. Quality Working Party (QWP)

Chair: Keith Pugh/Blanka Hirschlerova

Nomination of new core members to the QWP

• Abigail Moran (UK) – replacing Sean Jones

- Nomination Letter
- E-CV

• Maria Vassiliou (CY) – replacing Katerina Savvidou

- Nomination Letter
- E-CV

Action: For adoption

The CHMP nominated Abigail Moran and Maria Vassiliou as new core members to the QWP.

2.1.3. Scientific Advice Working Party (SAWP)

Chair: Robert Hemmings

No items

2.1.4. European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP)

Co-chair: Kaisa Immonen

No items

2.1.5. European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP)

Co-chair: Gonzalo Calvo

No items

2.1.6. Geriatric Expert Group (GEG)

Chair: Katarina Vučić

No items

2.1.7. Committees

HMPC and QWP: Guideline on quality of herbal medicinal products /traditional herbal medicinal products, DRAFT Revision 3 (EMA/CPMP/QWP/2819/00 Rev. 3)

Action: For adoption for 3 months public consultation

The third revision of the guideline takes into account new and revised guidelines, questions and answers and the European Pharmacopoeia revised general monograph 'Herbal Drug Extracts' as well as experiences gained over the years with the application of the guideline. Further clarifications on quality data requirements are provided via improved wording, structure and reference to updated related guidelines as outlined in the concept paper EMA/HMPC/217631/2015. Particular attention has been paid to adjustment with the in parallel revised Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and HMPs/THMPs (CPMP/QWP/2820/00; EMEA/CVMP/815/00, EMA/HMPC/162241/2005).

The CHMP adopted the guideline for 3 months public consultation.

HMPC and QWP: Guideline on specifications: test procedures and acceptance criteria for herbal substances , herbal preparations and herbal medicinal products /traditional herbal medicinal products, DRAFT Revision 3 (EMA/CPMP/QWP/2820/00 Rev. 3)

Action: For adoption for 3 months public consultation

The third revision takes into account new and revised guidance documents such as the updated 'Questions & Answers on quality of HMPs/THMPs' (EMA/HMPC/41500/2010), the European Pharmacopoeia revised general text on the 'Microbiological Quality of HMPs for Oral Use and Extracts used in their preparation' (5.1.8), the revised general Ph. Eur. monograph 'Herbal Drug Extracts' and the new information chapter on this monograph, the 'Guideline on quality on combination HMPs/THMPs' (MA/HMPC/CHMP/CVMP/214869/2006) and the 'Reflection paper on markers used for quantitative and qualitative analysis of HMPs/THMPs' (EMEA/HMPC/253629/2007) as outlined in the Concept paper EMA/HMPC/217753/2015. Particular attention has been paid to adjustment with the in parallel revised Guideline on quality of herbal medicinal products /traditional herbal medicinal products (EMA/CPMP/QWP/2819/00, EMA/CVMP/814/00, EMA/HMPC/201116/2005).

The CHMP adopted the guideline for 3 months public consultation.

SmPC Advisory Group: Proposal for the development of an eLearning product information review curriculum

Action: For discussion

Follow-up from June CHMP Plenary meeting

The CHMP noted the call for volunteers made. Further discussions are expected at the July CHMP Plenary and volunteers are invited to participate according to their expertise.

PDCO: Concept paper on the need for revision of the guideline on the investigation of medicinal products in the term and preterm neonate (EMA/PDCO/362462/2016)

Action: For adoption for public consultation

It was noted that there is a need to update currently available guidelines regarding the non-clinical and clinical development of medicinal products in neonates in accordance with current trends in neonatal terminology, and issues encountered and experience gained during assessment of several PIP applications involving neonatal population.

The preparation of guideline will involve the PDCO Neonatology Group and the PDCO with input from relevant working parties and committees. Drafts of the document will be discussed with the SAWP and other relevant working parties and committees. The CHMP was invited to send any comments.

The CHMP adopted the concept paper for public consultation.

2.1.8. International Council on Harmonisation (ICH)

No items

2.1.9. Joint CVMP/CHMP ad-hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in the regulatory testing of medicinal products (J 3RsWG)

Chair: Ellen-Margrethe Vestergaard, CoChair: Susanne Brendler-Schwaab

No items

2.1.10. Joint CHMP/CVMP/CMDh/CMDv Working Group on Active Substance Master File Procedures (ASMF WG)

Chair: Nienke Rodenhuis

No items

2.1.11. Joint CVMP-CHMP antimicrobial advice ad hoc expert group (AMEG)

Chair: Gérard Moulin

No items

2.1.12. Modelling and Simulation Working Party (MSWP)

Chair (acting): Kristin Karlsson/ Flora Musuamba Tshinanu

No items

2.2. Biologicals

2.2.1. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman

Guideline on similar biological medicinal products containing recombinant granulocyte-colony stimulating factor (rG-CSF) (EMA/483392/2018 Rev 1)

Action: For adoption

The CHMP noted the guideline. Further discussions can be expected at the July plenary and any comments should be sent to BMWP Secretariat.

2.2.2. Biologicals Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Final minutes from May face-to-face meeting held 22-23 May 2018 (EMA/CHMP/BWP/327614/2018)

Action: For information

The CHMP noted the final minutes.

Draft agenda for BWP face-to-face meeting to be held 10-12 September 2018 (EMA/CHMP/BWP/450681/2018)

Action: For information

The CHMP noted the final agenda.

Industry/regulators BWP/QWP Workshop on quality support to early access approaches (PRIME), which is being planned to take place on 26 Nov 2018 at the EMA (in London).

The aim of this workshop is to discuss with industry quality challenges during development of PRIME designated products due to shortened timelines and to identify scientific and regulatory approaches which could facilitate preparation of robust quality data packages at the time of submission of the MAA.

This workshop is intended to cover all product classes (chemical/biological/ATMP), in line with the PRIME-designated products, and it is also planned to involve SMEs and Big Pharma.

The workshop is being organised by an organising committee consisting of BWP, QWP, IWG experts and QoM colleagues. Five FDA colleagues representing chemical molecules, Biologicals and ATMPs have joined the organising committee and will also participate in the workshop.

The organising committee has prepared a first draft agenda (tabled), which has been endorsed by BWP, QWP and IWG, and would like to receive CHMP-ORGAM's agreement on this draft agenda in order to share it with industry stakeholders with the aim to invite case study proposals to be included under the respective scientific topics on the agenda.

Action: Draft agenda for agreement

The CHMP agreed to the draft agenda.

2.2.3. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

No items

2.2.4. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144533/2009 rev. 2)

Action: For adoption

Postponed to July Plenary.

Core SmPC for human plasma derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2)

Action: For adoption

Postponed to July Plenary.

2.2.5. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

No items

2.3. Therapeutics

2.3.1. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder/Alar Irs

No items

2.3.2. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

Guideline on clinical investigation of medicinal products in the treatment of epileptic disorders Rev. 3 (EMA/CHMP/264942/2017)

Action: For adoption for 6-months public consultation

Rapporteur André Elferink via TC

The main changes to the existing guideline include incorporation of the new classification / definitions of seizure types and epilepsies, the acceptance of add-on studies in support of a monotherapy claim on a case-by-case basis, the inclusion of new sections on neonates and status epilepticus and other changes related to paediatric developments.

This guideline provides assistance for the development and evaluation of medicinal products for the treatment of epilepsy in adults and children. The scope of this document is restricted to treatment of seizures in epileptic disorder although there are some remarks concerning non-seizure features of epilepsy syndromes.

The CHMP adopted the guideline for 6-months public consultation.

2.3.3. Infectious Diseases Working Party (IDWP)

Chair: Maria Jesus Fernandez Cortizo

No items

2.3.4. Oncology Working Party

Chair: Pierre Demolis/Paolo Foggi

Guideline on the use of minimal residual disease as a clinical endpoint in multiple myeloma studies (EMA/CHMP/183565/2018)

Action: For adoption for 3 months public consultation

Postponed to July Plenary

2.3.5. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Product-specific bioequivalence guidelines, batch 8 (final guidelines):

- Agomelatine oral tablet 25 mg product-specific bioequivalence guidance, EMA/CHMP/800802/2017
- Cholic acid capsules 50 mg and 250 mg product-specific bioequivalence guidance, EMA/CHMP/800759/2017
- Posaconazole gastro-resistant tablet 100 mg product-specific bioequivalence guidance, EMA/CHMP/800785/2017
- Ledipasvir/sofosbuvir film-coated tablet 90 mg/400 mg product-specific bioequivalence guidance, EMA/CHMP/800789/2017
- Vismodegib hard capsule 150 mg product-specific bioequivalence guidance, EMA/CHMP/800794/2017

Action: For adoption

The CHMP adopted the product-specific bioequivalence guidelines.

PKWP response to CMDh request on referral procedure vaginal ring

PKWP rapporteur: Sotiris Michaleas

Chair Jan Welink and Co-Chair Henrike Potthast will join

Action: For adoption

The CHMP discussed the response. The CHMP noted that the issue is not just a PK question. The CHMP adopted the response with further input in writing to be provided to reflect this point.

Jan Welink (Chair) representing CHMP at the 13th WRIB conference in New Orleans, LA, USA in April 1-5, 2019 .

Action: For adoption

The CHMP agreed to the participation.

Final minutes of the PKWP F2F meeting held 17-18 April 2018 (EMA/247464/2018)

Action: For information

The CHMP noted the final minutes.

2.3.6. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Jörg Zinserling

Creation of multidisciplinary drafting group for finalisation of "draft reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development" (EMA/CHMP/138502/2017) after public consultation

BSWP is seeking CHMP endorsement for the creation of a multi-disciplinary drafting group with members of BWP, BMWP, BSWP and QWP to finalise the draft reflection paper by the end of 2018.

Notes: The European Medicines Agency has published a reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development (EMA/CHMP/138502/2017), for a 1-year public consultation until 31 March 2018.

In total, 15 stakeholders provided extensive general and specific comments on the draft reflection paper comprising over 900 individual comments.

Further to the external consultation, the Agency held a multi-disciplinary scientific workshop with stakeholders from industry associations and international regulatory agencies on the 3rd and 4th of May 2018 to discuss comments received during the public consultation phase.

The organisation committee of the workshop - consisting of members of the BSWP, BMWP, BMWP, QWP - suggests that the finalisation of the reflection paper which touches upon quality, manufacturing, statistics, and methodology areas should be a shared responsibility between the respective working parties. BWP, BMWP, BSWP and QWP endorsed this proposal and will nominate a total of up to 10 working party members for the drafting group.

A finalisation of the reflection paper by the end of 2018 is envisaged with monthly and additional ad-hoc TCs planned as needed.

Action: For adoption

The CHMP agreed to the creation of multidisciplinary drafting group.

BSWP statement on Mahalonobis Distance (Original request from CMDh – input from PKWP and QWP) (EMA/810713/2017)

Action: For adoption

The CHMP adopted the BSWP statement for publication in the form of a question-and-answer document.

Nomination of new core member to BSWP

Action: For adoption

The CHMP nominated Christian B. (Kit) Roes as new core member to BSWP.

Questions and Answers on Data Monitoring Committee issues (EMA/479382/2018)
The aim of this question-and-answer document is to supplement the CHMP Data Monitoring Committee Guideline (EMEA/CHMP/EWP/5872/03) by providing clarification on the role and necessity for a Data Monitoring Committee (DMC) in different phases of drug development and throughout the product lifecycle as well as with regard to the responsibilities for implementing DMC decisions.

Action: For adoption for 1-year public consultation

The CHMP adopted the document for 1-year public consultation.

2.3.7. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Final minutes for RIWP meeting held by teleconference on 15 May 2018 (EMA/294067/2018)

Action: For information

The CHMP noted the minutes.

CMDh questions to RIWP and PKWP on Classification as Narrow Therapeutic Index (NTI) drug and advice on requirements for bioequivalence studies – colchicine (EMA/CMDh/455656/2018)

Action: For adoption

The CHMP adopted the questions to RIWP and PKWP.

Concept paper on the need to develop a reflection paper on development of medicinal products to prevent and treat acute kidney injury (EMA/CHMP/171100/2018)

Action: For re-adoption for public consultation

This is a correction to add "reflection of ICH E9 addendum on estimands".

The CHMP re-adopted the concept paper for public consultation.

2.3.8. Scientific Advisory Groups (SAGs)

No items

2.3.9. Drafting Groups (DGs)

2.3.9.1. Gastroenterology Drafting Group (GDG)

Chair: Mark Answorth

No items

2.3.9.2. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

No items

2.3.9.3. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

No items

2.3.9.4. Excipients Drafting Group

Chair: Dominique Masset

Final minutes from June face-to-face meeting held 12-13 June 2018 (EMA/430398/2018)

Action: For information

The CHMP noted the minutes.

2.3.10. Additional agenda points

2.3.10.1. Innovation Task Force

ITF Briefing Meeting

Meeting date: 5th September 2018

Action: For discussion and agreement

The CHMP agreed to the meeting.

Minutes from the meeting held on 25th June 2018

Action: For information

The CHMP noted the minutes.

Minutes from the meeting held on 14th March 2018.

Action: For information

The CHMP noted the minutes.

Minutes from the meeting held on 16th March 2018.

Action: For information

The CHMP noted the minutes.

Minutes from the meeting held on 20th March 2018.

Action: For information

The CHMP noted the minutes.

2.3.10.2. Guideline Consistency Group (GCG)

Chair: Barbara van Zwieten-Boot

Call for interest for a new Guideline Consistency Group Chair.

All GCG/CHMP/SAWP Members are eligible for the position of GCG Chairperson. Those who wish to apply for the Chairperson position are requested to submit a brief letter in support of their candidature together with a brief CV, highlighting the expertise.

Applications should be sent **by 17th July 2018**. Elections will take place at the July 2018 CHMP Plenary.

Action: For information

The CHMP noted the call.

2.3.10.3. IPRF Nano Working Group

Chair: Harald Enzmann/Jean Louis Robert

No items

3. Organisational, regulatory and methodological matters

3.1. Meeting organisation / templates

3.1.1. Final Rapporteur Assessment Report templates for Initial MAA and Generics applications

Follow-up from 22 March 2018 presentation and request for CHMP comments

Final track-changes documents following implementation of CHMP and PRAC members comments

Action: For information

The CHMP noted the final Rapporteur Assessment Report templates for Initial MAA and Generics applications. However, there were comments on geriatrics aspects needed in ARs, and it should be considered how to include proposed comments for ARs in this round of ARs templates update.

4. Any Other Business

4.1. Community Interests - Referral under Article 31 of Directive 2001/83/EC

4.1.1. Valsartan-containing medicinal products - EMEA/H/A-31/1471

MAHs: various

Rapporteur: TBC, Co-Rapporteur: TBC,

Scope: Start of procedure, list of questions, timetable, appointment of Rapporteurs

Action: For adoption

Referral notification from EC

The CHMP appointed Daniela Melchiorri as Rapporteur (interest level 2) and Martina Weise as Co-rapporteur (interest level 2).

The CHMP adopted a list of questions to the MAHs and API manufacturers with a specific timetable.

Notification: 5 July 2018

Start of the procedure (CHMP):16 July 2018

List of questions: 16 July 2018

Submission of responses: 30 July 2018

Re-start of the procedure: 23 August 2018

Rapporteur/Co-rapporteur assessment report(s) circulated to CHMP: 10 September 2018

Comments: 13 September 2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 14 September 2018

CHMP list of outstanding issues /CHMP opinion: 20 September 2018

There will be an ad-hoc expert consultation held.

Further updates to be presented to CHMP in July Plenary, including any updates on communication if necessary.

5. List of participants

CHMP Chair:

Tomas Salmonson

CHMP members:

Agnes Gyurasics

Daniela Melchiorri

Greg Markey

Harald Enzmann (Vice-Chair)

Jayne Crowe

Jan Mueller-Berghaus

Johann Lodewijk Hillege

Katarina Vučić

Robert James Hemmings

Simona Badoi

Svein Rune Andersen

CHMP alternate members:

Fátima Ventura

Dana Gabriela Marin

Mark Ainsworth

Milena Stain

Tuomo Lapveteläinen

Nithyanandan Nagercoil

Experts:

Anja Schiel

Eskild Colding-Jorgensen

Fabien Lavergne

Gloria Calderon de la Barca

Jan Welink

Henrike Potthast

Irene Diaz Ortiz

Keith Pugh

Kristina Bech Jensen

Maria Escudero Galindo

Milena Peraita Ezcurra

Representative from European Commission participated in the meeting.

The meeting was run with support from the relevant EMA staff