24 March 2022
EMA/CHMP/154439/2022
Human Medicines Division

Committee for medicinal products for human use (CHMP)

PROM[1] minutes for the meeting on 14 March 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

14 March 2022, 09:00–13:00, virtual meeting/room 08-A

Disclaimers

Some of the information contained in this document is considered commercially confidential or sensitive and therefore not disclosed.

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

Note on access to documents

Some documents mentioned in the agenda/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 PROM is a meeting to discuss CHMP organisational matters and other topics in preparation for the CHMP Plenary meeting. 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 PROM topics can be discussed at the CHMP Plenary.

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1. Agenda and Minutes

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting as well as the draft agenda of the plenary meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See March 2022 CHMP PROM minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agendas.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

1.2. Adoption of agenda

The CHMP adopted the PROM agenda for the 14 March 2022 meeting.

1.3. Adoption of the minutes

CHMP PROM Minutes of 14 March 2022 meeting will be adopted at the March 2022 CHMP plenary.

2. Non-therapeutic-area-specific working parties

2.1. Patients and Consumers Working Party (PCWP) Healthcare Professionals Working Party (HCPWP)

PCWP: Co-chair: Kaisa Immonen, Co-chair: Juan Garcia Burgos (EMA)

HCPWP: Co-chair: Ulrich Jaeger, Co-chair: Juan Garcia Burgos (EMA)

2.1.1. Nomination of representatives to the PCWP and HCPWP

Nomination of a representative (and alternate) for each working party for the mandate June 2022 to May 2025.

Action: For endorsement

CHMP noted the call for nominations for the representatives for the PCWP and HCPWP. Nominations should be sent.

2.2. Biologics Working Party (BWP)

Chair: Sol Ruiz

2.2.1. Agenda and minutes

- Draft agenda of BWP meeting to be held virtually on 14-16 March 2022
- Final minutes of BWP meeting held virtually on 17-19 January 2022

Action: For information

CHMP noted the agenda and the minutes.

2.2.2. Nomination of BWP members

- Nomination of Marie Louise Vindvad Kristensen as the BWP Member representing Denmark
- Nomination of Nanna Aaby Kruse (current Member) as the BWP Alternate representing Denmark

Action: For endorsement

CHMP endorsed the nominations of the BWP member and alternate from Denmark.

2.3. Quality Working Party (QWP)

Chair: Blanka Hirschlerova

2.3.1. Minutes

- Final minutes for QWP-CT meeting held virtually on 16 February 2022
- Final minutes from 98th QWP plenary meeting held virtually on 22-23 November 2021

Action: For information

CHMP noted the minutes.

2.3.2. Titanium Dioxide update

Update on workplan.

Action: For information

The CHMP noted the update on the titanium dioxide and the next steps.

The CHMP was reminded that the Commission Regulation (EU) 2022/63 of 14 January 2022 amending Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards the food additive titanium dioxide (the Regulation) has now entered into force following its publication in the Official Journal of the European Union on 18 January 2022. The next steps to support industry in replacing titanium dioxide (E 171) in medicinal products were noted by the CHMP.

2.4. Safety Working Party (SWP)

Chair: Susanne Brendler-Schwaab

2.4.1. Minutes

- Final minutes for SWP meeting held by teleconference on 19 January 2022

Action: For information

CHMP noted the minutes.

2.4.2. CMDh request on the AI for N-nitroso-salbutamol

The CMDh requests the SWP to determine the acceptable intake for N-nitroso-salbutamol based on lifetime daily exposure including information on the points of departure and methodology used.

In addition, the CMDh requests the SWP to consider if a class specific AI would be more appropriate for the N-nitrosamines with the substructure 1-[tert-butyl(nitroso)amino]-2-propanol (salbutamol-like).

Action: For adoption

CHMP endorsed the CMDh request on the AI for N-nitroso-salbutamol.

2.4.3. CMDh request on the AI for N-nitroso-sotalol

The CMDh requests the SWP to determine the acceptable intake for N-nitroso-sotalol based on lifetime daily exposure including information on the points of departure and methodology used.

In addition, the CMDh requests the SWP to consider if a class specific AI would be more appropriate for the N-nitrosamines with the substructure 1-[Isopropyl(nitroso)amino]-2-propanol (sotalol-like).

Action: For adoption

CHMP endorsed the CMDh request on the AI for N-nitroso-sotalol.

2.4.4. CMDh request on the AI for N-Nitroso-bumetanide

The CMDh requests the SWP to determine the acceptable intake for N-Nitroso-bumetanide based on lifetime daily exposure including information on the points of departure and methodology used.

Action: For adoption

CHMP endorsed the CMDh request on the AI for N-Nitroso-bumetanide.

2.4.5. Requests for CHMP/EMA external representation

- Request from SWP member Sonja Beken to represent CHMP/EMA at the European Partnership for Alternative Approaches to Animal Testing (EPAA) Steering Committee meeting on 24 March 2022 via Webex to present the EMA's Innovation Task Force initiative on 3Rs.
- Request from SWP member Sonja Beken to represent CHMP/EMA at the European Partnership for Alternative Approaches to Animal Testing (EPAA) Partners Forum on

'Exposure considerations for human safety assessment' scheduled on 5 May 2022 in Brussels to present the experience from the point of view of the EMA the use of exposure data in non-clinical risk assessment.

Action: For adoption

CHMP endorsed the request from SWP member Sonja Beken to represent CHMP/EMA at the European Partnership for Alternative Approaches to Animal Testing (EPAA) Steering Committee meeting on 24 March 2022 and to represent CHMP/EMA at the European Partnership for Alternative Approaches to Animal Testing (EPAA) Partners Forum on 'Exposure considerations for human safety assessment' scheduled on 5 May 2022.

2.5. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz

2.5.1. Agenda and minutes

- Agenda of BMWP meeting held virtually on 02 March 2022
- Final minutes of BMWP meeting held virtually on 17 November 2021

Action: For information

CHMP noted the agenda and the minutes.

2.6. Biostatistics Working Party (BSWP)

No topics

2.7. Modelling and Simulation Working Party (MSWP)

No topics

2.8. Pharmacogenomics Working Party (PGWP)

No topics

2.9. Pharmacokinetics Working Party (PKWP)

Chair: Carolien Versantvoort

2.9.1. Product-specific guidelines

Revision of product-specific guidelines

- Ibuprofen oral use immediate release formulations 200 - 800 mg product-specific bioequivalence guidance (EMA/CHMP/356876/2017) Revision 1
- Paracetamol oral use immediate release formulations product-specific bioequivalence guidance (EMA/CHMP/356877/2017) Revision 1
- Tadalafil film-coated tablets 2.5 mg, 5 mg, 10 mg and 20 mg product-specific bioequivalence guidance (EMA/CHMP/315234/2014/Rev.1) Revision 2

Action: For adoption

The CHMP were informed about revisions of the guidelines on Ibuprofen oral use immediate release formulations 200 - 800 mg, on Paracetamol oral use immediate release formulations and Tadalafil film-coated tablets 2.5 mg, 5 mg, 10 mg and 20 mg. The guidelines have been revised to define the maximum acceptable difference for T_{max} medians. The CHMP adopted the guidelines for 3-month public consultation.

2.9.2. CMDh Question to PKWP on Interpretation of the Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms

In the February 2022 CMDh meeting, the CMDh discussed comments raised on the interpretation of the Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms (EMA/CHMP/EWP/280/96 Rev1). In order to come to a harmonised EU position in this respect, the CMDh has agreed to forward a question to PKWP.

Action: For adoption

The CHMP endorsed the consultation of PKWP.

3. Therapeutic-area-specific working parties and SAGs

3.1. Blood Products Working Party (BPWP)

Chairs: Jacqueline Kerr/Karri Penttilä

3.1.1. Agenda and minutes

- Agenda of the Blood Cluster TC to be held virtually on 18 March 2022

Action: For information

The CHMP noted the agenda.

3.2. Central Nervous System Working Party (CNSWP)

No topics

3.3. Cardiovascular Working Party (CVSWP)

No topics

3.4. Infectious Diseases Working Party (IDWP)

No topics

3.5. Oncology Working Party (ONCWP)

Chair(s): Vacant

3.5.1. Call for nominations for ONCWP member

Following the resignation of Sinan B. Sarac, nominations for a new ONCWP member were requested.

Action: For information

CHMP noted the nominations received. Further discussion is expected at the March Plenary.

3.6. Rheumatology/Immunology Working Party (RIWP)

No topics

3.7. Vaccines Working Party (VWP)

No topics

3.8. Scientific Advisory Groups (SAGs)/Ad-hoc Expert Groups (AHEGs)

3.8.1. Proposal for single nominated chairperson for all AHEGs

A proposal from EMA for a single nominated AHEG chairperson.

Action: For adoption

CHMP noted the proposal from EMA for a single nominated AHEG chairperson.

Overall, the CHMP supported the proposal for a single nominated AHEG chairperson. Further discussion is expected at a future PROM.

4. Drafting groups

4.1. Excipients Drafting Group

No topics

4.2. Gastroenterology Drafting Group (GDG)

No topics

4.3. Geriatric Expert Group (GEG)

No topics

4.4. Radiopharmaceuticals Drafting Group (RadDG)

No topics

4.5. Respiratory Drafting Group (RDG)

No topics

5. Harmonisation and consistency groups

5.1. International Council on Harmonisation (ICH)

5.1.1. Nomination of experts for ICH group

Quality Discussion Group (QDG).

Action: For adoption

CHMP endorsed the nomination of Sean Barry (IE) to replace Nanna Aaby Kruse (DK) as BWP representative and Regulatory Chair of the Quality Discussion Group (QDG).

5.1.2. ICH Q2(R2) – Validation of analytical methods

Step 2b - ICH Q2(R2) to be adopted for a 4-month public consultation.

Action: For adoption

CHMP adopted the Step 2b - ICH Q2(R2) for a 4-month public consultation.

5.1.3. ICH Q14 – Analytical procedure development

Step 2b - ICH Q14 to be adopted for a 4-month public consultation.

Action: For adoption

CHMP adopted the Step 2b - ICH Q14 for a 4-month public consultation.

5.1.4. ICH E11A – Paediatric extrapolation

Step 2b - ICH E11A to be adopted for a 4-month public consultation.

Action: For adoption

CHMP adopted the Step 2b - ICH Q14 for a 4-month public consultation.

5.1.5. ICH Q3D(R2) – Guideline for elemental impurities

Step 5 - The ICH Q3D(R2) Regulatory experts are completing the step 3 sign-off of the guideline and the Regulatory Members of the Assembly will be invited to adopt as final under Step 4 this document, which would subsequently be published on the ICH public website. The guideline will be implemented 6 months after adoption.

Action: For adoption

CHMP adopted the ICH Q3D(R2) – Guideline for elemental impurities to be implemented 6 months after adoption.

5.2. Guideline Consistency Group (GCG)

No topics

5.3. Summary of product characteristics Advisory Group

No topics

6. Joint groups and collaboration with other Scientific committees

6.1. 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)

No topics

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

No topics

6.3. Collaboration with other Scientific committees

6.3.1. PRAC report to CHMP

Chair: Sabine Straus

Summary of recommendations and advice of PRAC meeting held on 07-10 March 2021.

Action: For information

The CHMP noted the summary of recommendations and advice.

7. Regulatory/Organisational matters

7.1. Regulatory Issues/new legislation

7.1.1. Pharma Strategy

Revision of the Pharmaceutical legislation: update

Action: For discussion

The CHMP noted the proposals and proposed amendments for consideration.

7.2. CHMP organisation/templates

7.2.1. CHMP learnings

Collection, discussion and recording of CHMP learnings

CHMP: Outi Mäki-Ikola

Action: For discussion

CHMP endorsed the proposed learnings.

7.2.2. CHMP co-opted membership

The 3-year co-opted member mandate for Christian Gartner comes to an end on 23.06.2022. His area of expertise is medical statistics.

The nomination procedure foresees that the CHMP should decide on whether a new co-opted member should be appointed and if so, on the required specific complementary scientific expertise (there could be more than one area). Afterwards a call for nominations will be launched.

Action: For information

CHMP noted that the 3-year co-opted member mandate for Christian Gartner comes to an end on 23.06.2022. CHMP agreed on the need to fill the 5th co-opted member position. The next discussion on the area of expertise is expected at the April PROM. Proposals can be sent in advance of the meeting **by 6 April, EOB**.

8. Product development support

8.1. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

8.1.1. Appointment of CHMP peer review for SA

Action: For information

The CHMP noted the report.

8.1.2. Nomination of new member and alternate to the Scientific Advice Working Party

Nomination of new SAWP member and alternate.

The required areas of expertise: oncology, genetic disorders (focus on metabolic and neurological ones), infectious diseases, clinical trial methodology and/or pharmacoepidemiology.

Nomination(s) received.

Action: For endorsement

CHMP endorsed the nomination of Cristina Migali as member and Anja Schiel as alternate to the SAWP.

8.1.3. Call for nominations for Scientific Advice Working Party vice-chair(s)

The second mandate of Scientific Advice Working Party vice-chair Peter Mol will expire in May 2022.

Action: For information

CHMP noted the call for nominations for the SAWP vice-chair(s).

8.2. Innovation Task Force

8.2.1. ITF meeting

Meeting date: 25 March 2022

Action: For information

CHMP endorsed the meeting.

8.2.2. ITF meeting

Meeting date: 28 March 2022

Action: For adoption

CHMP endorsed the meeting.

8.2.3. ITF meeting

Meeting date: 01 April 2022

Action: For adoption

CHMP endorsed the meeting.

9. Product related topics

9.1. Preview CHMP Plenary

CHMP: Harald Enzmann

Action: For information

Some procedures on the agenda of the upcoming plenary meeting were flagged.

9.2. COVID-19 ongoing and upcoming procedures

List of currently ongoing and upcoming (imminently, i.e. expected within the next 2 months) applications for COVID-19 vaccines and therapeutics.

Action: For information

CHMP noted the Covid-19 ongoing and upcoming procedures.

9.3. Synchron Research Services – various – EMEA/H/A-31/1515

Article 31 procedure triggered by the Federal Agency for Medicines and Health Products (FAMHP) in Belgium, the Danish Medicines Agency (DKMA), the Finnish Medicines Agency (Fimea), the Medicines Evaluation Board (MEB) in the Netherlands and the Medical Products Agency (MPA) in Sweden concerning the contract research organisation (CRO) Synchron Research Services, located in Ahmedabad, Gujarat, India.

Referral Rapporteur: Kristina Dunder, Referral Co-Rapporteur: Janet Koening

Scope: List of questions to PKWP

Action: For adoption

The CHMP adopted the list of questions to PKWP.

The CHMP was reminded of the adopted timetable:

Re-start of the procedure: 25 March 2022

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 28 April 2022

Comments: 06 May 2022

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 12 May 2022

CHMP list of outstanding issues/CHMP opinion: May 2022 CHMP

10. Any Other Business

10.1. Data protection notice (DPN) – processing of scientific Committees (CxMP) members/alternates' contact details

Introduction of the DPN, developed to allow to share CXMP contact details in MMD.

Action: For information

CHMP noted the introduction of the DPN, developed to allow to share CXMP contact details in MMD.

10.2. Rapporteurships

Update.

Action: For information

CHMP noted the update.

11. List of Participants

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda and for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Helena Panayiotopoulou	Member	Cyprus	No interests declared	
Thalia Marie Estrup Blicher	Alternate	Denmark	No restrictions applicable to this meeting	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantina Alexopoulou	Member	Greece	No interests declared	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Jan Sjöberg	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Armando Genazzani	Member	Italy	No interests declared	
Maria Grazia Evandri	Alternate	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting	COVID-19 vaccines
Martine Trauffler	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Ingrid Wang	Member	Norway	No interests declared	
Eva Skovlund	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting	COVID-19 vaccines

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda and for which restrictions apply
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriel Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Dorota Distlerova	Alternate	Slovakia	No interests declared	
Kristina Nadrah	Member	Slovenia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Christian Gartner	Co-opted member	Austria	No interests declared	
Carla Torre	Co-opted member	Portugal	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czechia	No interests declared	
Alfredo García-Arieta	Expert - via WebEx*	Spain	No interests declared	
Deirdre Mannion	Expert - via WebEx*	Denmark	No restrictions applicable to this meeting	
Kristin Karlsson	Expert - via WebEx*	Sweden	No restrictions applicable to this meeting	
Paula Contreras Alarcón	Expert - via WebEx*	Spain	No restrictions applicable to this meeting	
Maria Victoria Tudanca Pacios	Expert - via Webex*	Spain	No restrictions applicable to this meeting	
Mas Parra Paloma	Expert - via WebEx*	Spain	No restrictions applicable to this meeting	
Luca Santi	Expert - via WebEx*	Italy	No restrictions applicable to this meeting	
Martina Perini	Expert - via WebEx*	Italy	No restrictions applicable to this meeting	
Theis Moeslund Jensen	Expert - via WebEx*	Denmark	No restrictions applicable to this meeting	
Nora Cascante Estepa	Expert - via WebEx*	Germany	No interests declared	
Carolien Versantvoort	Expert - via WebEx*	Netherlands	No interests declared	
Irene Bachmann	Expert - via WebEx*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda and for which restrictions apply
Sabine Mayrhofer	Expert - via WebEx*	Germany	No interests declared	
Vincent Gazin	Expert - via WebEx*	France	No interests declared	
Meeting run with the help of EMA staff				

*Experts were evaluated against the product(s) they have been invited to talk about.