22 May 2015
EMA/CHMP/290828/2015
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Minutes of meeting held on 20-23 April 2015

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

20 April 2015, 13:00 – 19:00, room 2A

21 April 2015, 08:30 – 19:45, room 2A

22 April 2015, 08:30 – 19:45, room 2A

23 April 2015, 08:30 – 12:00, room 2A

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present following a request for access to documents under 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).

Health & 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 and therefore not disclosed. With regards to therapeutic indications 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. The procedures discussed by the CHMP are on-going and therefore are considered confidential. Additional details on some of these procedures will be published in the CHMP meeting

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highlights once the procedures are finalised and start of referrals will also be available. For orphan medicinal products the applicant details are published as this information is already publicly available. Of note, this agenda is a working document primarily designed for CHMP members and the work the Committee undertakes.

Further information with relevant explanatory notes can be found at the end of this document.

For adoption

Agenda (EMA/CHMP/206325/2015 rev.4) and Annex to CHMP agenda of the CHMP plenary session to be held 20-23 April 2015.	The agenda and annex were adopted with amendments.
Timeschedule (EMA/CHMP/223425/2015 rev.3) of the CHMP plenary session to be held 20-23 April 2015.	The timeschedule was adopted.
Minutes ((EMA/CHMP/223528/2015 rev. 0) of the CHMP plenary session held 23-26 March 2015.	The Minutes of the CHMP plenary session held 23 – 26 March 2015 were adopted.

For information

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 20-23 April 2015	*See April 2015 Minutes (to be published post May 2015 CHMP meeting)* The pre-meeting list was noted.
Draft Agenda of CHMP meeting to be held on 18-21 May 2014.	The draft agenda was noted.

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1. Oral explanations

1.1. Pre-authorisation procedure oral explanations

(EMEA/H/C/003766), (evolocumab), (Hypercholesterolaemia and mixed dyslipidaemia and Homozygous familial hypercholesterolaemia)
List of Questions adopted on 22.01.2015.
An oral explanation was held on Tuesday 21 April 2015 at 11.00.
See section 2.2. Initial applications; Day 180 List of outstanding issues

(EMEA/H/C/003702), (phenylephrine hydrochloride / ketorolac trometamol), (maintenance of intraoperative mydriasis, prevention of intraoperative miosis and reduction of acute postoperative ocular pain in intraocular lens replacement (ILR) in adults)
List of Outstanding Issues adopted on 22.05.2014. List of Questions adopted on 23.01.2014.
An oral explanation was held on Wednesday 22 April 2015 at 11.00.

1.2. Re-examination procedure oral explanation

No item

1.3. Post-authorisation procedure oral explanation

Somavert (EMEA/H/C/000409/X/0072), (pegvisomant), MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Arnaud Batz, "Addition of 25 mg and 30 mg powder and solvent for solution for injection."
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 25.09.2014.
The CHMP agreed that no oral explanation was needed at this time.
See also section 3.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 List of outstanding issues

1.4. Referral procedure oral explanation

No item

2. Initial applications

2.1. Initial applications; Opinions

Aripiprazole Pharmathen (EMEA/H/C/003803), (aripiprazole), Applicant: Pharmathen S.A., Generic of Abilify, (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 20.11.2014.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The Committee noted the letter of recommendation dated 17.04.2015.
The summary of opinion was circulated for information.

Aripiprazole Zentiva (EMEA/H/C/003899), (aripiprazole), Applicant: Zentiva, a.s., Generic of Abilify, (treatment of schizophrenia and prevention of manic episodes in bipolar I disorder)
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 20.11.2014.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Lympreva (EMEA/H/C/002772), Orphan, (dasiprotimut-t), Applicant: Biovest Europe Ltd, (treatment of non-Hodgkin's lymphoma (FL))
New active substance (Article 8(3) of Directive No 2001/83/EC)
Oral explanation was held on 24 March 2015. List of Outstanding Issues adopted on 18.12.2014.
List of Questions adopted on 25.04.2014.
The members were reminded of previous discussions.
The Committee adopted a negative opinion by consensus together with the CHMP assessment report.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The refusal question-and-answer document was circulated for information.
The Committee adopted the BWP Report.

Duloxetine Mylan (EMEA/H/C/003981), (duloxetine), Applicant: GENERICS (UK) LIMITED
Generic of Cymbalta,(treatment of major depressive disorder, diabetic peripheral neuropathic pain and generalised anxiety disorder)
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 22.01.2015.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Hetlioz (EMEA/H/C/003870), Orphan, (tasimelteon), Applicant: Vanda Pharmaceuticals Ltd., (treatment of Non-24-Hour Sleep-Wake Disorder (Non-24))
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 25.09.2014.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
Furthermore, the CHMP considered that tasimelteon is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Lixiana (EMEA/H/C/002629), (edoxaban), Applicant: Daiichi Sankyo Europe GmbH, , (prevention of stroke; embolism and treatment of venous thromboembolism)
New active substance (Article 8(3) of Directive No 2001/83/EC)
Oral explanation was held on 24 February 2015. List of Outstanding Issues adopted on 26.02.2015, 22.01.2015, 20.11.2014.
List of Questions adopted on 26.06.2014.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
Furthermore, the CHMP considered that edoxaban is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The Committee noted the letter of recommendation.
The summary of opinion was circulated for information.

LuMark (EMEA/H/C/002749), (lutetium, isotope of mass 177), Applicant: I.D.B. Radiopharmacy B.V., (used only for the radiolabelling of carrier molecules)
Well-established use application (Article 10a of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 26.06.2014.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to restricted medical prescription.
The summary of opinion was circulated for information.

Opdivo (EMEA/H/C/003985), (nivolumab), Applicant: Bristol-Myers Squibb Pharma EEIG, , (treatment of advanced (unresectable or metastatic) melanoma in adults.)
New active substance (Article 8(3) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 22.01.2015.
The Committee discussed, whether conditional or full approval should be granted and whether patient subpopulations that mostly benefited from treatment could be distinguished according to biomarkers.
The Committee also discussed the product information and Annex II conditions.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
Furthermore, the CHMP considered that nivolumab is a new active substance, as claimed by the applicant.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to restricted medical prescription.
The summary of opinion was circulated for information.
The Committee adopted the BWP Report.

Pregabalin Mylan (EMEA/H/C/004078), (pregabalin), Applicant: Generics (UK) Limited, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Mylan Pharma, (treatment of epilepsy and generalised anxiety disorder (GAD))
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 18.12.2014.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Pregabalin Mylan Pharma (EMEA/H/C/003962), (pregabalin), Applicant: Generics UK Limited, Generic, Generic of Lyrica, (treatment of neuropathic pain, epilepsy and generalised anxiety disorder (GAD))
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 18.12.2014. The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The summary of opinion was circulated for information.

Pregabalin Sandoz (EMEA/H/C/004010), (pregabalin), Applicant: SANDOZ GmbH, Generic of Lyrica, (treatment of neuropathic pain, epilepsy and generalised anxiety disorder)
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 18.12.2014.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The Committee noted the letter of recommendation dated 15.04.2015.
The summary of opinion was circulated for information.

Pregabalin Sandoz GmbH (EMEA/H/C/004070), (pregabalin), Applicant: SANDOZ GmbH, Generic of Lyrica, Duplicate of Pregabalin Sandoz, (treatment of epilepsy and generalised anxiety disorder (GAD))
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 18.12.2014.
The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The legal status was agreed as medicinal product subject to medical prescription.
The Committee noted the letter of recommendation dated 15.04.2015.
The summary of opinion was circulated for information.

2.2. Initial applications; Day 180 List of outstanding issues

(EMEA/H/C/003935), (duloxetine), (Treatment depressive disorder, diabetic neuropathic pain, anxiety disorder, treatment depressive disorder, diabetic neuropathic pain, anxiety disorder)
List of Questions adopted on 22.01.2015.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003820), (pembrolizumab), (treatment of melanoma)
List of Questions adopted on 23.10.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

(EMEA/H/C/002792), Orphan, (susoctocog alfa), Applicant: Baxter AG, (treatement of haemophilia A)
List of Questions adopted on 20.11.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues,
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.
Furthermore the CHMP adopted a List of Questions to the BPWP.

(EMEA/H/C/002839), (sonidegib), (treatment of basal cell carcinoma (BCC))
List of Questions adopted on 25.09.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a list of Outstanding Issues with a specific timetable.

(EMEA/H/C/003766), (evolocumab), (Hypercholesterolaemia and mixed dyslipidaemia and Homozygous familial hypercholesterolaemia)
List of Questions adopted on 22.01.2015.
See section 1.1. Pre-authorisation procedure oral explanations.
An oral explanation was held on Tuesday 21 April 2015 at 11.00 focusing on the target patient population as well as the wording of the indication.
The CHMP adopted a list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

(EMEA/H/C/002739), (human alpha1-proteinase inhibitor), (treatment of lung disease)
The ad-hoc expert group meeting held on 14 January 2015.
List of Outstanding Issues adopted on 26.03.2015 and 20.11.2014. List of Questions adopted on 25.04.2014.
The Committee was reminded of the status of this application and its remaining outstanding issues.
The CHMP adopted a 3rd list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

2.3. Initial applications; Day 120 List of Questions

(EMEA/H/C/003898), (brivaracetam), (treatment of partial-onset seizures)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/004042), (elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide), (treatment of HIV-1)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/004104), (eptifibatide), (prevention of early myocardial infarction)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/002733), (ferric maltol), (treatment of iron deficiency anaemia)
The Committee noted the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/004147), (octocog alfa), (treatment and prophylaxis of haemophilia A, treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency))
The Committee noted the issues identified in this application,
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/003825), (octocog alfa), (treatment and prophylaxis of haemophilia A, treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency))
The Committee noted the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/002790), (opicapone), (Parkinson's disease and motor fluctuations)
The Committee noted the issues identified in this application,
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/004114), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003886), (necitumumab), (treatment of squamous non-small cell lung cancer)
The Committee noted the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/003882), (alirocumab), (reduction of low-density lipoprotein cholesterol (LDL-C) and increase high-density lipoprotein cholesterol (HDL-C).)
The Committee noted the issues identified in this application.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

The Committee adopted the BWP Report.

(EMEA/H/C/004004), Orphan, (sebelipase alfa), Applicant: Synageva BioPharma Ltd(treatment of enzyme replacement therapy (ERT))
The Committee noted the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/004007), (etanercept), (treatment of arthritis)
The Committee noted the issues identified in this applicationThe Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.
The Committee adopted the BWP Report.

(EMEA/H/C/003774), Orphan, (selexipag), Applicant: Actelion Registration Ltd., (treatment of pulmonary arterial hypertension (PAH; WHO Group I))
The Committee noted the issues identified in this application
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

2.4. Update on on-going initial applications for Centralised procedure

(EMEA/H/C/003938), (betulae cortex dry extract (5-10 : 1); extraction solvent: n-heptane 95% (w/w)), (treatment of partial thickness wounds)
The CHMP agreed to the request by the applicant for an extension of clock stop to submit the responses to the D120 List of Questions, with a specific timetable.
The CHMP adopted the CHMP Similarity Assessment Report.

(EMEA/H/C/003790), Orphan (Carfilzomib), Applicant: Amgen Europe B.V., (treatment of multiple myeloma),
The CHMP adopted the CHMP Similarity Assessment Report.

(EMEA/H/C/003750), Orphan, ATMP, (allogenic human heterologous liver cells), Applicant: Cytonet GmbH&Co KG, (treatment of urea cycle disorders (UCD)),
List of Outstanding Issues adopted on 18.12.2014. List of Questions adopted on 25.04.2014.
The CHMP was updated on the discussions at the CAT regarding the oral explanation held during the April Plenary meeting

(EMEA/H/C/003776), (ferric citrate coordination complex), (treatment of hyperphosphataemia)
List of Questions adopted on 24.07.2014. List of Outstanding Issues adopted on 26.03.2015
The CHMP agreed to the request by the applicant for an extension of the clock-stop for submission of responses to Day 180 List of Outstanding Issues with a specific timetable.

(EMEA/H/C/003759), (guanfacine), (treatment of ADHD)
List of Questions adopted on 24.07.2014.
The CHMP adopted a List of Questions to SAG Psychiatry

(EMEA/H/C/003725), Orphan, (panobinostat), Applicant: Novartis Pharmaceuticals UK Limited, (treatment of multiple myeloma)

List of Questions adopted on 25.09.2014.
The CHMP adopted the List of experts to SAG Oncology meeting

(EMEA/H/C/003926), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
The Committee was updated on the procedure.

(EMEA/H/C/003914), (human fibrinogen / human thrombin), (supportive treatment for improvement of haemostasis and as a suture support in vascular surgery)
List of questions adopted in February 2015.
The CHMP agreed to the request by the applicant for an clock stop to respond to the List of Questions adopted in February 2015 with a specific timetable.

(EMEA/H/C/002616), Orphan, (pitolisant hydrochloride), Applicant: BIOPROJET PHARMA, (treatment of narcolepsy)
The members noted the letter from the applicant informing that the consolidated responses to ASMF List of Questions will be submitted at the next procedural step, i.e. Day 180 List of Outstanding Issues.

(EMEA/H/C/004008), (aripiprazole), (treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 20.11.2014.
The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 180 List of Outstanding Issues adopted in March 2015 with a specific timetable.

(EMEA/H/C/003905), (pemetrexed), (treatment of malignant pleural mesothelioma and non-small cell lung cancer)
List of Questions adopted on 26.02.2015.The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 120 List of Questions adopted in February 2015 with a specific timetable.

(EMEA/H/C/003861), Orphan, (parathyroid hormone), Applicant: NPS Pharma Holdings Limited, (treatment of hypoparathyroidism)
List of Questions adopted on 26.03.2015The CHMP noted the amended PI to the Day 120 List of Questions.

(EMEA/H/C/002801), Orphan, ATMP, (allogeneic t cells genetically modified to express suicide gene), Applicant: MolMed SpA, (treatment in haploidentical haematopoietic stem cell transplantation)
List of Outstanding Issues adopted on 26.03.2015. List of Questions adopted on 24.07.2014.
The CHMP noted that the CAT has agreed at their April Plenary meeting to the request by the applicant for an extension of clock stop to respond to the Day 180 List of Outstanding Issues with a specific timetable.

(EMEA/H/C/003936), (amikacin), (treatment of Pseudomonas aeruginosa lung infection/colonisation in cystic fibrosis patients treatment of nontuberculous mycobacterial lung infection)
The CHMP adopted a request for supplementary information on the assessment of similarity via written procedure on 24 April 2015 together with a specific timetable.

(EMEA/H/C/003954), Orphan, (lumacaftor / ivacaftor), A (treatment of cystic fybrosis)

2.5. Products in the Decision Making Phase

No item

3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

3.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinions

Orfadin (EMEA/H/C/000555/X/0041), Orphan, (nitisinone), MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, PRAC Rapporteur: Carmela Macchiarulo, "To add an oral suspension 4 mg/ml as additional pharmaceutical form"
List of Outstanding Issues adopted on 23.10.2014. List of Questions adopted on 19.12.2013.
The Committee confirmed that all issues previously identified in this application had been addressed.
The Committee adopted a positive opinion by consensus, together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The Committee noted the letter of recommendation dated 20.04.2015.

3.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 List of outstanding issues

Somavert (EMEA/H/C/000409/X/0072), (pegvisomant), MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Arnaud Batz, "Addition of 25 mg and 30 mg powder and solvent for solution for injection."
List of Outstanding Issues adopted on 26.02.2015. List of Questions adopted on 25.09.2014.
The CHMP agreed that no oral explanation was needed at this time.
See also section 1.3 Post-authorisation procedure oral explanation.
The Committee was reminded of the status of this application and its remaining outstanding issues.The Committee concluded that the Major objection regarding the representativeness of the bio-batch tested according to the BE guidelines was cancelled. The analysed batch was considered representative of the full scale production batch.
The CHMP adopted a 2nd list of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Similarity Report.

3.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of Questions

Emend (EMEA/H/C/000527/X/0049/G), (aprepitant), MAH: Merck Sharp & Dohme Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Pieter de Graeff, PRAC Rapporteur: Ulla Wändel Liminga, "The MAH has submitted a type II variation classified as C.I.6 to extend the indication for chemotherapy-induced nausea and vomiting (CINV) in adults to paediatric patients (12 to 17years) for the 80mg and 125mg hard capsules. SmPC section 4.2 and 5.3 of the 165mg hard capsule label, which is consequential to the outcome of this grouped procedure, will be updated under the scope of type II variation classified as C.I.6.
In addition to this, an application for an addition of a new pharmaceutical form (powder for oral suspension) has been submitted for 125mg stength as part of this grouping.
The MAH has also submitted a type II variation classified as C.I.4 to reflect the paediatric results for prevention of post-operative nausea and vomiting (PONV) in the clinical sections of 40mg hard capsules label, thus updating sections 5.1 and 5.2 of the SmPC.
The Package Leaflet has been proposed to be updated accordingly."
The Committee discussed the issues identified in this application, mainly relating to the process validation.
The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

3.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No item

4. Type II variations - Extension of indication procedures according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Type II variation; Extension of indication- Opinions or Requests for supplementary information

Esmya (EMEA/H/C/002041/II/0028), (ulipristal), MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.1 of the SmPC with subsequent updates to sections 4.2, 4.4, 4.8 and 5.1 in order to extend the current indication to intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 26.02.2015, 20.11.2014.
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.

Invega (EMEA/H/C/000746/II/0043), (paliperidone), MAH: Janssen-Cilag International N.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "Update of sections 4.1 of the SmPC in order to extend the Invega indication to include depressive symptom domain of schizoaffective disorder. Additionally section 5.1 has been updated to reflect the data from the study SCA-3004 on paliperidone palmitate effects in the maintenance of symptom control. Minor editorial changes have been introduced throughout the PI. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."
Request for Supplementary Information adopted on 20.11.2014.
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.

Kuvan (EMEA/H/C/000943/II/0033), Orphan, (sapropterin), MAH: Merck Serono Europe Limited, Rapporteur: Patrick Salmon, Co-Rapporteur: Daniel Brasseur, "Extension of indication for the 'treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have shown to be responsive to such treatment' to include the paediatric population under 4 years old. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated accordingly."
Request for Supplementary Information adopted on 26.02.2015
The Committee discussed the issues identified in this application, mainly relating to the measuring device for the paediatric population.
The CHMP agreed not to consult the QWP at this stage.
The Committee adopted a Request for Supplementary Information with a specific timetable.

Levemir (EMEA/H/C/000528/II/0071), (insulin detemir), MAH: Novo Nordisk A/S, Rapporteur: Jens Heisterberg, Co-Rapporteur: Pieter de Graeff, "Extension of indication to use levemir in combination with GLP-1 receptor agonists for the treatment of type 2 diabetes mellitus. Consequently, the MAH proposed the update of sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC. The Package Leaflet is updated in accordance.
The variation proposed amendments to the Summary of Product Characteristics and Package Leaflet."
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.

Pyramax (EMEA/H/W/002319/II/0002), (pyronaridine / pyronaridine phosphate / artesunate), MAH: Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Arnaud Batz, "x To amend SmPC section 4.1 (Therapeutic Indications) to remove restrictions on repeated course of treatment in any individual and use only in areas of low transmission with evidence of artesmisinin resistance, based on further clinical experience. Consequent changes in SmPC sections 4.2 (Posology), 4.4 (Special warnings and precautions), 4.8 (Undesirable effects) and the PL are also included. A recommended change is made to SmPC Section 4.2 (Posology) in relation to dosing in mild to moderate renal impairment. A minor editorial adjustment is proposed to SmPC section 5.1 (Pharmacodynamic properties)."
Request for Supplementary Information adopted on 18.12.2014, 26.06.2014.
The CHMP noted the report from the SAG anti-infectives meeting held on 30 March 2015.

The Committee discussed the issues identified in this application. There was a consensus from the SAG that there was sufficient evidence gained to use Pyramax in asymptomatic patients without systematic liver testing, provided that an effective RMP should be put in place, including appropriate pharmacovigilance measures and a commitment of a phase IV study to be carried out in order to undertake enhanced real-life safety surveillance under enlarged conditions (notably retreatment, co-infection, no systematic liver testing). The experts reached consensus that in view of the short treatment duration, no stopping rules can be formulated for emerging signs /symptoms of liver injury, except anaphylaxis. Also treatment should not be started in those with known underlying hepatic injury. Thus, retreatment in the affected community would therefore be permitted unless the patient had clinical jaundice or known severe liver disease (decompensated cirrhosis, Child-Pugh stage 3 or 4) at time that new course is required. The Committee concluded that the product could be approvable, provided that satisfactory responses are provided to the third RSI mainly covering the need for a revised RMP (including a proposal for a phase IV study as identified as critical during the SAG meeting to enable deriving further reassurance on the use of Pyramax under enlarged conditions and a revised SPC.
The Committee adopted a 3rd Request for Supplementary Information with a specific timetable.

Relistor (EMEA/H/C/000870/II/0030), (methylnaltrexone bromide), MAH: TMC Pharma Services Ltd, Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Valerie Strassmann, "The MAH applied for an extension of the indication for the treatment of opioid induced constipation in adult non cancer pain patients. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC. The Package Leaflet was proposed to be updated in accordance."
Request for Supplementary Information adopted on 26.03.2015, 20.11.2014, 26.06.2014.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.
The CHMP agreed by consensus on 1-year extension of market exclusivity.

Resolor (EMEA/H/C/001012/II/0034), (prucalopride), MAH: Shire Pharmaceuticals Ireland Ltd., Rapporteur: Greg Markey, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Rafe Suvarna, "The Marketing authorisation holder (MAH) applied for a new indication to extend the indication into the male population based on data from study SPD555-302. Consequently, the MAH proposed the update of sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC. The Package Leaflet was proposed to be updated in accordance."
Request for Supplementary Information adopted on 18.12.2014.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.
The members discussed the acceptability of the additional 1-year market protection.

The CHMP agreed by consensus on 1-year extension of market exclusivity.

Revlimid (EMEA/H/C/000717/II/0079), Orphan, (lenalidomide), MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Arnaud Batz, "Extension of Indication to add treatment of adult patients with relapsed and/ or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised version of the RMP (version 25.0) was provided as part of this application." Request for Supplementary information adopted on 26.03.2015.
The Committee discussed the issues identified in this application. The members noted that one question was omitted in the RSI adopted in March 2015 although it was reflected in the discussion part of the Assessment Report. The RSI was therefore updated accordingly.
The Committee adopted a revised Request for Supplementary Information with a specific timetable.

Tygacil (EMEA/H/C/000644/II/0092), (tigecycline), MAH: Pfizer Limited, Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Miguel-Angel Macia, "Addition of a new restricted indication in children eight year-old and older. The sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated accordingly. The Package Leaflet is also updated. In addition, an updated RMP is proposed." Request for Supplementary Information adopted on 26.03.2015.
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.
The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.
The summary of opinion was circulated for information.

Vidaza (EMEA/H/C/000978/II/0030), Orphan, (azacitidine), MAH: Celgene Europe Limited, Rapporteur: Pieter de Graeff, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Sabine Straus, "Extension of Indication to add treatment of adult patients aged 65 years or older who are not eligible for HSCT with AML with >30% marrow blasts according to the WHO classification, based on the pivotal phase III study AZA- AML-001. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. A revised RMP version 10.0 was provided as part of the application. The application includes a request for an additional year of market protection for a new indication in accordance with Article 10(1) of Directive 2001/83/EC."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)
The Committee discussed the issues identified in this application. The discussions focused on the efficacy results as well as the request for 1 year market protection.
The Committee adopted a Request for Supplementary Information with a specific timetable.

4.2. Update on on-going type II variation; extension of indications

Qutenza (EMEA/H/C/000909/II/0039), (capsaicin), MAH: Astellas Pharma Europe B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Magda Pedro, , "Extension of indication to include treatment of diabetic patients with peripheral neuropathic pain based on the results of studies E05-CL-3004 (STEP) and E05-CL-3002 (PACE). As a consequence sections 4.1, 4.4 and 4.8 of the SmPC have been updated, and Annex II (additional risk minimisation measures) and the Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II, labelling and Package Leaflet. An updated RMP (version 18) was provided as part of the application. The provision of studies STEP and PACE addresses MEA 001.4."
The CHMP agreed to the request by the applicant for an extension of clock stop to submit the responses to the Request for Supplementary Information adopted on 23.03.2015 with a specific timetable.

5. Ancillary medicinal substances in medical devices

5.1. Ancillary medicinal substances in medical devices - Opinions/ List of outstanding issues / List of Questions

(EMEA/H/D/003740), (human serum albumin), (the storage, manipulation, in-vitro culture and transfer of human gametes)
List of Outstanding Issues adopted on 26.02.2015, 18.12.2014, 25.09.2014.
List of Questions adopted on 23.01.2014.
The Committee discussed the issues identified in this application.
The Committee confirmed that all issues previously identified in this application had been resolved.
The Committee adopted a positive Opinion by consensus together with the CHMP assessment report.
The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.
The Committee adopted the BWP Report.

6. Re-examination procedure (new applications) under Article 9(2) of Regulation no 726/2004

No item

7. Re-examination procedure (Type II variations) under Article 16 of Commission Regulation (EC) No 1234/2008 and 9(2) of Regulation (EC) No 726/2004

No item

8. Withdrawal of full initial application

Duloxetine Sandoz (EMEA/H/C/004009), (duloxetine), Applicant: SANDOZ GmbH (treatment in adults of major depressive disorder, diabetic peripheral neuropathic pain and generalised anxiety disorder.)
Generic application (Article 10(1) of Directive No 2001/83/EC)
List of Questions adopted in January 2015.

The CHMP noted the Letter from the applicant dated 08.04.2015 informing of the withdrawal of the marketing authorisation application together with the EMA withdrawal question and answer document.

9. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No item

10. Pre-submission issues

Some items in this section are considered commercially confidential or sensitive and therefore not disclosed.

(H0003854) (Autologous CD34+ Cells Transduced with Retroviral Vector Containing the Adenosine Deaminase Gen), (Severe combined immunodeficiency due to adenosine deaminase deficiency),
ATMP
The CHMP noted the CAT recommendation on the request for accelerated assessment

11. Post-authorisation issues

Some items in this section are considered commercially confidential or sensitive and therefore not disclosed.

WS0689/G

TECFIDERA-EMEA/H/C/002601/WS0689/0011/G

NAPs included in WS: Fumaderm, Fumaderm Intial (fumarate containing products), MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 of the SmPC in order to add a recommendation to consider interruption of treatment in patients with low lymphocyte counts (<0.5 x 109/L) persisting for more than six months and to monitor lymphocyte counts until recovery. Update of section 4.8 of the SmPC with information on observed low lymphocyte counts in clinical studies with tecfidera and PML (Progressive multifocal leukoencephalopathy) occurrence in the setting of severe and prolonged lymphopenia. Furthermore, the due dates of two commitments as part of the RMP have been revised." Request for Supplementary information adopted on 26.02.2015.
The Committee discussed the issues identified in this application concerning the available data on PML. The Committee agreed to consult a SAG.
The Committee adopted a 2nd Request for Supplementary Information with a specific timetable.
The CHMP adopted a List of Questions to the SAG Neurology. Additional experts will be identified to participate in the SAG meeting.

Infanrix hexa (EMEA/H/C/000296) (Diphtheria Toxoid Adsorbed,Filamentous Haemagglutinin,Pertussis Toxoid Adsorbed,Poliovirus Type 1 (Inactivated),Poliovirus Type 2 (Inactivated),Poliovirus Type 3 (Inactivated),Pertactin,Tetanus Toxoid Adsorbed,Haemophilus Influenzae Type B Polysaccharide, Adsorbed,Hepatitis B, Recombinant Surface Antigen, Adsorbed), MAH: GlaxoSmithKline Biologicals, Rapporteur: Daniel Brasseur, Co-Rapporteur: Jan Mueller-Berghaus,
The CHMP adopted the letter to GSK Biologicals concerning the batch release testing and the application of 3Rs methods.

Hexacima (EMEA/H/C/002702) (diphtheria (d), tetanus (t), pertussis (acellular, component) (pa), hepatitis b (rdna) (hbv), poliomyelitis (inactivated) (ipv) and haemophilus influenzae type b (hib) conjugate vaccine (adsorbed)), MAH: Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniel Brasseur,
The CHMP adopted the letter to Sanofi Pasteur concerning the batch release testing and the application of 3Rs methods.

Bronchitol (EMEA/H/C/001252/II/0016/G), Orphan, (mannitol), MAH: Pharmaxis Pharmaceuticals Limited, Rapporteur: Robert James Hemmings, "Update of the condition reported in annex II D of the product information in order to update the protocol condition on patients recruitment and consequentially to postpone the final study report due date.
The Committee confirmed that all issues previously identified in this application ad been addressed.
The Committee adopted a positive opinion by consensus together with the CHMP Assessment report and Translation timetable.
The Icelandic and Norwegian members were in agreement with the CHMP recommendation.

Glybera (EMEA/H/C/002145/II/0038), Orphan, (alipogene tiparvovec), MAH: uniQure biopharma B.V., Rapporteur: Elaine French, CHMP Co-ordinator: Greg Markey, "Update of section 5.1 of the SmPC based on the final CSR for Study CT-AMT-011-05, a retrospective clinical records review study undertaken to generate further long-term follow-up data on the incidence and severity of acute pancreatitis episodes in LPLD subjects who previously participated in clinical studies with alipogene tiparvovec or AMT-10."Request for Supplementary Information adopted on 20.11.2014.
The Committee was updated on the discussions from the April CAT Plenary meeting.
The Committee agreed to the 2nd Request for Supplementary Information as adopted at the CAT together with a specific timetable.

Daklinza (EMEA/H/C/003768) (Daclatasvir Dihydrochloride), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings, (treatment of chronic hepatitis C virus)

Harvoni (EMEA/H/C/003850) (sofosbuvir+ledipasvir), MAH: Gilead Sciences International, Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich, (treatment of chronic hepatitis C)

Sovaldi (EMEA/H/C/003850) (sofosbuvir), MAH: Gilead Sciences International, Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, treatment of chronic hepatitis C)
The CHMP was updated on the discussion at the PRAC concerning a signal of arrhythmia. The CHMP discussed the difference of intense monitoring versus close monitoring. A DHPC letter was discussed and agreed by the Committee.

PROVENGE (EMEA/H/C/002513), (Autologous Peripheral Blood Mononuclear Cells Activated With Pap-Gm-Csf (Sipuleucel-T)), Dendreon UK LTD, Rapporteur: Egbert Flory, Co-Rapporteur: Nicolas Ferry, CHMP Coordinator of the Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator of the Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC Co-Rapporteur: Arnaud Batz,
The CHMP noted the letter from the MAH informing about the withdrawal of the marketing authorisation.

12. Referral procedures

12.1. Procedure for Centrally Authorised products under Article 20 Council Regulation (EC) No 726/2004

No item

12.2. Requests for CHMP Opinion under Article 5(3) and 57 (1)p of Regulation (EC) No 726/2004

No item

12.3. Procedure under Articles 5(2) and 10 of the Regulation (EC) No 726/2004

No item

12.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC

MERISONE 50 mg and 150 mg film coated tablets and MYOSON 50 mg and 150 mg film coated tablet (EMEA/H/A-29/1411)

(tolperisone)

Applicant /MAH: Meditop Pharmaceutical Co.Ltd.

Rapporteur: Agnes Gyurasics , Co-Rapporteur: Johann Lodewijk Hillege, RMS: HU, CMS: DE, NL, BE, LU, Mutual recognition procedures: HU/H/0373/001-002/MR and HU/H/0377/001-002/MR

Scope: Lack of bioequivalence studies to evaluate the food effect.

List of Questions adopted 22.01.2015.

The Committee concluded the grounds for positive opinion and revised the divergent position. The Committee noted that because the characteristics of the active substance of Merisone and Myoson food will affect the absorption of the active substance in the same way as for Mydeton and no further studies are required. The CHMP therefore concluded that in the case of Merisone and Myoson the bioequivalence study in the fasting state is sufficient to conclude on the bioequivalence in both the fasting and fed states and that the benefits and risks of Merisone and Myoson can be taken to be the same as the reference medicine's.

The CHMP adopted an opinion by majority (21 positive out of 32 votes) recommending that the objections raised by Germany should not prevent the granting of a marketing authorisation. The assessment report was adopted.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The divergent position (Pierre Demolis, Alar Irs, Daniela Melchiorri, Greg Markey, Harald Enzmann, Hubert Leufkens, Jan Mueller-Berghaus, Ondrej Slanaer, Pieter de Graeff, Robert Hemmings, Romaldas Maciulaitis) was appended to the opinion.

The CHMP noted the EMA question-and-answer document.

12.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

Haldol and associated names (EMEA/H/A-30/1393) (haloperidol), Janssen-Cilag Group of companies and associated companies
Rapporteur: Martina Weise, Co-Rapporteur: Ivana Mikacic,
The CHMP agreed to the request for extension of clock stop to respond to the List of Outstanding Issues adopted in March 2015 with a specific timetable.
List of outstanding issues (LoOI): March 2015 CHMP; Responses to LoOI: 04.09.2015; Restart of the procedure: 22.09.2015; Assessment report: 07.10. 2015; Comments from CHMP: 12.10.2015; List of outstanding issues 2 or CHMP opinion: October 2015 CHMP

Haldol decanoate and associated names (EMEA/H/A-30/1405) (haloperidol) Janssen-Cilag Group of companies and associated companies
Rapporteur: Martina Weise, Co-Rapporteur: Ivana Mikacic,
The CHMP agreed to the request for extension of clock stop to respond to the List of Outstanding Issues adopted in March 2015 with a specific timetable.
List of outstanding issues (LoOI): March 2015 CHMP; Responses to LoOI: 04.09.2015; Restart of the procedure: 22.09.2015; Assessment report: 07.10. 2015; Comments from CHMP: 12.10.2015; List of outstanding issues 2 or CHMP opinion: October 2015 CHMP

Novantrone and associated names (EMEA/H/A-30/1399) (mitoxantrone), MEDA group of companies and associated companies.
Rapporteur: Pieter de Graeff, Co-Rapporteur: Robert Hemmings,
Harmonisation exercise for Novantrone and associated names. The review was triggered by the European Commission, due to the need of harmonisation of the Summary of Product Characteristics across Member States.
The CHMP agreed to the request for extension of clock stop to respond to the List of Outstanding Issues adopted in March 2015 with a specific timetable.
Submission of responses: 18.05.2015; Re-start of the procedure: 23.06.2015; Joint Rapporteurs assessment report circulated to CHMP: 08.07.2015; Comments: 13.07.2015; List of outstanding issues/CHMP opinion: July 2015 CHMP

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

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097)
Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff,
CHMP granted an extension of the deadline to submit FUM 001 related to study evaluating the potential for long-term retention of gadolinium in bone until 8th April 2015
The CHMP was updated on the responses received from the company.
The CHMP agreed to consult the PRAC with possible further involvement of the SAWP.

Adrenaline auto injectors (EMEA/H/A-31/1398)
Rapporteur: Alar Irs, Co-Rapporteur: Robert James Hemmings,
Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients. List of Outstanding Issues adopted on 25.09.2014 and 26.02.2015.
The CHMP was informed of discussions at the PRAC and noted the advice to the CHMP.

12.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

GVK Biosciences (EMEA/H/A-31/1408)

Re-examination Rapporteur: Hubert Leufkens, re-examination Co-Rapporteur: Karsten Bruins Slot, Article 31 procedure triggered by the European Commission concerning GVK Biosciences Private Limited (GVK Bio), Swarna Jayanthi commercial complex, Ameerpet, Hyderabad 500 038, India following critical GCP deficiencies reported during an inspection performed by the ANSM (Agency for Medicines and Health Products Safety, France) on 19-23 May 2014. Opinion adopted on 22.01.2015. The CHMP noted the letters of intent and detailed grounds for re-examination.

12.8. Procedure under Article 107(2) of Directive 2001/83/EC

No item

12.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) (EC) No 1084/2003)

No item

12.10. Procedure under Article 29 Regulation (EC) 1901/2006

No item

12.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) No 1234/2008)

No item

13. Pharmacovigilance issues

Summary of recommendations and advice of PRAC meeting held on 7-10 April 2015: **For information**	The Committee noted the report. The members noted the Summary of recommendations and advices of the PRAC meeting.
List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2015: **For adoption**	The EURD list was adopted.
Early Notification System: April 2015 Early Notification System on Envisaged CHMP Recommendations for Regulatory Action (based on Identified Safety Concerns) Accompanied by Communication to the General Public: **for information**	See individual items

14. Inspections

14.1. GMP inspections

Disclosure of information related to GMP inspections will not be published as it undermines the purpose of such inspections.

14.2. GCP inspections

Disclosure of information related to GCP inspections will not be published as it undermines the purpose of such inspections.

14.3. Pharmacovigilance inspections

Disclosure of information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections.

14.4. GLP inspections

Disclosure of information related to GLP inspections will not be published as it undermines the purpose of such inspections.

15. Innovation Task Force

15.1. Minutes of Innovation Task Force: For information

15.2. Briefing meetings (Innovation Task Force)

Disclosure of information related to briefing meetings taking place with applicants cannot be released at present time as deemed to contain commercially confidential information.

15.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004

No item

15.4. Nanomedicines activities

No item

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 7-10 April 2015. Table of conclusions: **For information**	The CHMP noted the report.
Scientific advice letters:	*Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.*

17. Satellite Groups

17.1. Coordination Group for Mutual Recognition and Decentralised Procedures

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 20-22 April 2015: **For information**	The CHMP noted the report.
CMDh question to CHMP (PKWP, SWP) regarding potential risk of longer half-life of acitretin, • PKWP / SWP position: **For adoption**	The CHMP discussed the draft PKWP/SWP responses and agreed to bring this back to PKWP for further consideration on an acitretin threshold considering the detection limits
CMDh request dated 14 April 2015 for advice from PKWP regarding classification of everolimus in transplant setting as narrow therapeutic index drug: **For discussion** • Scientific statement : **For information**	The CHMP noted the request from the CMDh and agreed for the PKWP to be contacted on the classification of everolimus in transplant setting as narrow therapeutic index drug.

18. Other Committees

Update on outcome of CVMP referral on lidocaine: **For information**	The members were updated on the outcome of the CVMP referral on lidocaine.

18.1. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 14-16 April 2015: **For information**	To be sent in the Post-mail.

18.2. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on9-12 March 2015: **For information**	To be sent in the Post-mail.

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2015 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 15-17 April 2015: **For information**	The CHMP noted the report.

18.4. Committee for Advanced Therapies (CAT)

Draft Minutes of CAT meeting held on 16-17 April 2015: **For information**	The CHMP noted the draft Minutes.

19. Invented name issues

Table of Decisions of the NRG meeting held in March 2015: **For adoption**	The CHMP adopted the Table of Decision of the NRG meeting.

20. Any other business

Proposal for a pre-marketing risk-based model for medicinal product testing – Pilot procedure: **For adoption**	The CHMP noted the proposal for a pre-marketing risk-based model for medicinal product testing. A 6-month pilot was proposed to include MRP, DCP, CAP products validated between July and December 2015. It was estimated to involve around 700 MRPs/DCPs and 64 new centralised MAAs. The Quality Assessors will be expected to complete a Risk-Assessment Template and Testing recommendations for each new application, by Day 80 of the procedure. Concern was expressed on the magnitude of the pilot considering the totality of data. An interim analysis was proposed with an update to the CHMP. Furthermore the possibility to share the workload between the NCAs and EMA will be further explored. The CHMP agreed to start the pilot.
Update on activities related to revised RMP Assessment process in 2015 • Implementation of the revised RMP assessment process: **For discussion**	The CHMP was given an update on the revised RMP assessment process. The members noted that a more detailed document on the practicalities of CHMP/PRAC collaboration will be circulated shortly.

CHMP representatives at the Pharmacovigilance Implementation Group • Invitation to an additional CHMP representative to join the Group: **For discussion**	Additional CHMP representative is called to join the Implementation Group, who would track progress on implementation, co-ordinate the IT work and ensure that lessons learnt and opportunities for improvement are discussed and presented to the ERMS-FG. The time allocated to the work by the representative, is 1 teleconference (TC) per week, 1 TC lasts up to 2 hours. The mandate lasts until the end of year. Nominations for an additional CHMP representative should be sent.
Committees' harmonised agenda template: **For information**	The CHMP noted the new harmonised agenda template. The new template will be implemented from May 2015 onwards. In 6 months a review of the new template will be done and discussed with the Committees.
Proposal for update of the use of conditional Marketing Authorisation • Reflection paper: **For discussion** • Proposal for update of Draft CHMP Guideline on conditional marketing authorisation: **For discussion** • Summary of CHMP reflections on Conditional MA for EC expert group STAMP: **adopted**	The CHMP noted the topics of discussion identified by CHMP sponsors and EMA, and the proposal for an update of the draft CHMP Guideline on conditional marketing authorisation. The CHMP agreed on a summary document to be provided for the European Commission expert group STAMP meeting in May 2015.
Revision of the Guideline on clinical development of fixed combination medicinal products: **For adoption for 6-month public consultation**	This guideline replaces 'Guideline on clinical development of fixed combination medicinal products' (CHMP/EWP/240/95 Rev. 1). The CHMP adopted the revision of the guideline for 6-month public consultation.
Blood Products Working Party Outline for EMA Workshop to be held on 1-2 July 2015 on Haemophilia Registries: **For adoption**	This initiative provides an appropriate starting point to consider what regulators need from haemophilia registries. The aim is to get the best capture of data in the EU and build on existing expertise in this area. It is proposed to work with stakeholders on this topic, commencing with this EMA workshop. The CHMP adopted the report on the workshop for publication on the EMA website.
Letter to DG ENV relating to the non-technical project summaries that companies provide when seeking authorisation for approval of an animal test: **For agreement**	The letter suggests including a cross reference to relevant Ph Eur monograph where relevant

Criteria for competence and experience of Committee members - for recommendation to NCAs in appointment process	The CHMP noted the criteria for competence and experience of Committee members - for recommendation to NCAs in appointment process. The CHMP and PRAC were invited to review the proposal for criteria and areas of expertise and to determine the need for additions or modifications.
Cardiovascular Working Party Draft Reflection paper on assessment of cardiovascular risk of medicinal products for the treatment of cardiovascular and metabolic diseases (EMA/CHMP/50549/2015): **For adoption for 3 month public consultation**	The draft reflection paper to be sent to the PRAC for information and comments and to be re-discussed at May ORGAM and if adopted put for public consultation after that.
Quality Working Party Guideline on Manufacture of the Finished Dosage Form (EMA/CHMP/QWP/BWP/245074): **For adoption for 6-month public consultation**	This guideline replaces the note for guidance on the manufacture of the finished dosage form. The note for guidance has been updated to reflect changes to the format and content of the Common Technical Document (CTD) Module 3 dossier. It also addresses current manufacturing practices in terms of complex supply chains and worldwide manufacture. In addition, the content and principles of the ICH Q8 guideline (ref 1) is also taken into account. The CHMP adopted the guideline for 6-month public consultation.
Concept paper on the development of a guideline on quality and equivalence of topical products (EMA/CHMP/QWP/245108/2015): **For information**	The assessment of topical product has evolved and it has become evident that their quality needs to be thoroughly understood and characterised, supported by a robust manufacturing process and control strategy. In addition, the designated shelf life needs to be based not only on physical, chemical and microbiological stability, but also, when necessary, on evidence of stable *in vitro* performance to assure equivalence throughout storage. The CHMP noted the concept paper.
Nomination of Hrefna Gudmundsdóttir (IS) as an observer for the Rheumatology/Immunology Working Party: **For information**	The CHMP noted the nomination as observer
Nomination of Guenter Waxenecker (AGES) as Alternate EU Topic leader for the Expert Working Group working on ICH S5(R2): **For adoption**	The CHMP endorsed Guenter Waxenecker as Alternate EU Topic leader for the Expert Working Group working on ICH S5(R2).

Questions and Answers on Benzalkonium chloride in the context of the revision of the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (CPMP/463/00) • Overview of comments from public consultation: **For adoption** • Final Background review: **For adoption**	The CHMP adopted the Overview of comments from public consultation and the Final Background review.
Agenda on Bacteriophage therapy workshop, to be held on 8 June 2015, at EMA 09:00 – 16:15 (UK time): **For information**	The CHMP noted the agenda
Dutch take the lead on biosimilar switching (Scrip article): **For information**	Hubert Leufkens commented briefly on the recent MEB statement on interchangeability of biosimilars as also reported in Scrip. Guidance on biosimilar prescribing is a national responsibility; in some of the scientific discussions on biosimilars, at the CHMP meeting reference was made to practice implementation.

21. List of participants

List of participants including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 20-23 April 2015 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Daniel Brasseur	Member	Belgium	No interests declared	
Bart Van der Schueren	Alternate	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Ana Dugonjić	Alternate	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No participation in discussions, final deliberations and voting on:	- Aripiprazole Zentiva (EMEA/H/C/003899), (aripiprazole) - Aripiprazole Pharmathen (EMEA/H/C/003803), (aripiprazole)
Jens Heisterberg	Member	Denmark	No restrictions applicable to this meeting	
Christian Schneider	Alternate	Denmark	No interests declared Also connected via TC	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Pierre Demolis	Member (Vice-Chair)	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No restrictions applicable to this meeting	
Agnes Gyurasics	Member	Hungary	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No restrictions applicable to this meeting	
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Pieter de Graeff	Member	Netherlands	No interests declared	
Johann Lodewijk Hillege	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Dinah Duarte	Alternate	Portugal	No interests declared	
Nela Vilceanu	Member	Romania	No interests declared	
Jan Mazag	Member	Slovakia	No interests declared	
Ivana Pankuchova	Alternate	Slovakia	No interests declared	
Nevenka Tršinar	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Arantxa Sancho-Lopez	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Rafe Suvarna	Alternate	United Kingdom	No interests declared	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Hubert Leufkens	Co-opted member	Netherlands	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Ana Alonso Gutierrez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Barbara Bannister	Expert - in person*	United Kingdom	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Alexandre Moreau	Expert - in person*	France	No interests declared	
Illiana Meurs	Expert - in person*	Netherlands	No interests declared	
Madli Pintson	Expert - in person*	Estonia	No interests declared	
Peter Mol	Expert - via telephone*	Netherlands	No interests declared	
Anneliese Hilger	Expert - via telephone*	Germany	No interests declared	
Nuria Prieto	Expert - via telephone*	Spain	No interests declared	
Mirza Catibusic	Expert - via telephone*	Ireland	No interests declared	
Lies (Elizabeth) Van Vlijmen	Expert - via telephone*	Netherlands	No interests declared	
Gedske Thomsen	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Amany N. El-Gazayerly	Expert - via telephone*	Netherlands	No interests declared	
Karri Penttilä	Expert - in person*	Finland	No interests declared	
Clemens Mittmann	Expert - via telephone*	Germany	No interests declared	
John Johnston	Expert - in person*	United Kingdom	No interests declared	
Zoran Simic	Expert - in person*	United Kingdom	No interests declared	
Yolanda Barbachano	Expert - in person*	United Kingdom	No interests declared	
Terry Shepard	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Christophe Focke	Expert - in person*	Belgium	No interests declared	
Deirdre O'Regan	Expert - via telephone*	Ireland	No interests declared	
Bengt Ljungberg	Expert - via telephone*	Sweden	No interests declared	
Frank Holtkamp	Expert - via telephone*	Netherlands	No interests declared	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Paolo Foggi	Expert - via telephone*	Italy	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 1)*

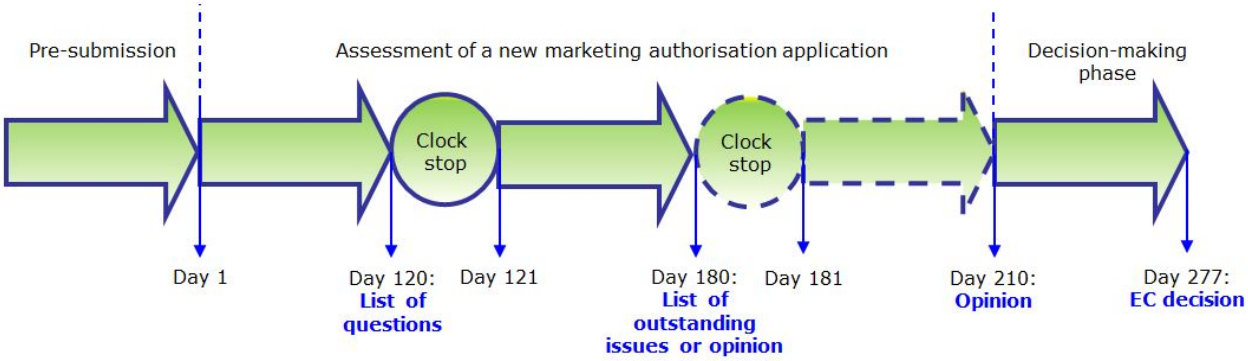
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section 12) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

New applications *(section 2)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 2.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 2.2 (**Day 180 List of outstanding issues**) and 2.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 2.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 2.5, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 3)*

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 4)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 3. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 5)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 6)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section 7)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 8)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 9)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 10)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 11)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 12)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 13)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 14)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 15)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 16)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 17)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 18)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.