25 September 2014
EMA/CHMP/614190/2014
Procedure Management and Business Support Division

Committee for medicinal products for human use (CHMP)

Minutes of meeting held on 22-25 September 2014

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

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).

Disclaimers

Some of the information contained in this agenda 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 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.

Agenda (EMA/CHMP/465006/2014) and Annex to CHMP agenda of the CHMP plenary session to be held 22-25 September 2014.	The agenda and annex were adopted with amendments.

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Timeschedule of the CHMP plenary session to be held 22-25 September 2014	The timeschedule was adopted.
Minutes of the CHMP plenary session held 21-24 July 2014 (EMA/CHMP/471144/2014)	The Minutes of the CHMP plenary session held 21-24 July 2014 were adopted via written procedure on 01 October 2014.
Minutes of the September 2014 CHMP ORGAM meeting held on 15 September 2014 (EMA/CHMP/433531/2014)	The Minutes of the September 2014 CHMP ORGAM meeting held on 15 September 2014, together with all decisions taken at that meeting, were adopted via written procedure on 01 October 2014.
Membership Announcement	The Committee noted that Maria Popova-Kiradjieva was nominated as the new Bulgarian CHMP alternate, replacing Lyubina Todorova in this role as of 30 July 2014. Furthermore Daniela Melchiorri and Luca Pani changed role. Prof Melchiorri is the new Italian member and Prof Pani the new Italian alternate as of 4 September 2014.
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 22-25 September 2014.	See September 2014 minutes (to be published post October 2014 CHMP meeting) The pre-meeting list was noted.
Draft Agenda of CHMP plenary to be held on 20-23 October 2014	The draft agenda was noted.

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1. Oral explanations

1.1. Pre-authorisation procedure oral explanations

(EMEA/H/C/003726), Orphan, (olaparib), Applicant: AstraZeneca AB, (treatment of ovarian cancer) List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 23.01.2014. The CHMP noted the SAG report. The CHMP agreed that no oral explanation was needed at this time. The CHMP adopted a 2nd List of Outstanding Issues with a specific timetable.

Cyramza (EMEA/H/C/002829), Orphan, (ramucirumab), Applicant: Eli Lilly Nederland B.V., (treatment of gastric cancer), New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 23.01.2014. An oral explanation was held on Tuesday 23 September 2014 at 11.00.
See also section 2.1 opinions

(EMEA/H/C/002548), Orphan, (afamelanotide), Applicant: Clinuvel (UK) Limited, (treatment of phototoxicity in adult patients with erythropoietic protoporphyria (EPP)), List of Outstanding Issues adopted on 23.01.2014, 21.03.2013. List of Questions adopted on 19.07.2012. An oral explanation was held on Tuesday 23 September 2014 at 14.00. Patient representatives were involved. During oral explanation the applicant introduced the positive patient experiences and positive clinical effect of the medicine. The Committee discussed the methodological issues related to study design.
The CHMP adopted a List of Outstanding Issues with a specific timetable.

(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 24 September 2014 at 9.00. During the oral explanation the applicant emphasized the clinical benefit. The Committee discussed the safety issues related to sterilisation process. The CHMP adopted a 2nd List of Outstanding Issues with a specific timetable. The CHMP agreed to consult an ad-hoc expert group on safety issues. A list of questions to the ad-hoc expert group will be adopted via written procedure.

(EMEA/H/C/002314), (bazedoxifene / estrogens conjugated), (treatment of oestrogen deficiency) List of Outstanding Issues adopted in March, June 2014. List of Questions adopted in November 2012. An oral explanation was held on Wednesday 24 September 2014 at 11.00. During the oral explanation the applicant introduced revised indication and addressed the issue on endometrial safety. The Committee discussed the endometrial safety further. The wording of the indication was also discussed.

Lymphoseek (EMEA/H/C/002085), (tilmanocept), Applicant: Navidea Biopharmaceuticals Limited, (used in the delineation and localisation of lymph nodes)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 20.03.2014, 19.12.2013, 24.10.2013. List of Questions adopted on 30.05.2013. The CHMP noted the SAG report. The CHMP agreed that no oral explanation was needed at this time.
See also 2.1 New applications - Opinions

1.2. Re-examination procedure oral explanation

Avastin (EMEA/H/C/000582/II/0059), (bevacizumab), MAH: Roche Registration Ltd, "Extension of indication to include Avastin in combination with radiotherapy and temozolomide for the treatment of adult patients with newly diagnosed glioblastoma." Opinion adopted on 22.05.2014. An oral explanation was held on Monday 22 September 2014 at 14.00.
See also 7. Re-examination procedure (type II variations)

1.3. Post-authorisation procedure oral explanation

Javlor (EMEA/H/C/000983/II/0011), (vinflunine ditartrate), MAH: Pierre Fabre Médicament, Rapporteur: Greg Markey, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Julie Williams, "Extension of Indication: in combination with capecitabine for the treatment of adult patients with locally advanced or metastatic breast cancer not amenable to curative surgery or radiotherapy, who are capecitabine and vinca alkaloid naïve, and were previously treated with or resistant to an anthracycline and who are taxane resistant." Request for Supplementary Information adopted on 25.04.2014, 19.09.2013. Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004). An oral explanation was held on Tuesday 23 September 2014 at 9.00.
See also section 4.1 Opinions or Requests for Supplementary information – Type II variation; Extension of indication

1.4. Referral procedures oral explanations

No items

2. New applications

2.1. Opinions – New full applications

Brimica Genuair (EMEA/H/C/003969), (aclidinium / formoterol fumarate dihydrate), Applicant: Almirall S.A, Duplicate, Duplicate of Duaklir Genuair, (maintenance bronchodilator treatment for airflow obstruction and relief of symptoms in adult patients with chronic obstructive pulmonary disease (COPD))
Fixed combination application (Article 10b of Directive No 2001/83/EC), List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.03.2014. The Committee adopted a positive opinion by majority (27 positive out of 29 votes) recommending the granting of a marketing authorisation together with the CHMP assessment report and translation timetable. The legal status was agreed as medicinal product subject to medical prescription. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Daniela Melchiorri and Concepcion Prieto Yerro) was appended to the opinion. The summary of opinion was circulated for information.

Duaklir Genuair (EMEA/H/C/003745), (aclidinium / formoterol fumarate dihydrate), Applicant: Almirall S.A, (treatment of chronic obstructive pulmonary disease (COPD))
Fixed combination application (Article 10b of Directive No 2001/83/EC), List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.03.2014. The Committee adopted a positive opinion by majority (27 positive out of 29 votes) recommending the granting of a marketing

authorisation together with the CHMP assessment report and translation timetable. The legal status was agreed as medicinal product subject to medical prescription. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Daniela Melchiorri and Concepcion Prieto Yerro) was appended to the opinion. The summary of opinion was circulated for information.

Budesonide/Formoterol Teva (EMEA/H/C/003951), (budesonide / formoterol), Applicant: Teva Pharma B.V., (treatment of asthma and chronic obstructive pulmonary disease (COPD))
Hybrid application (Article 10(3) of Directive No 2001/83/EC), List of Questions adopted on 24.07.2014. 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.

Vylaer Spiromax (EMEA/H/C/003952), (budesonide / formoterol), Applicant: Teva Pharma B.V., (treatment of asthma and chronic obstructive pulmonary disease (COPD))
Hybrid application (Article 10(3) of Directive No 2001/83/EC), List of Questions adopted on 24.07.2014.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.

Budesonide/Formoterol Teva Pharma B.V. (EMEA/H/C/003953), (budesonide / formoterol), Applicant: Teva Pharma B.V., (treatment of asthma)
Hybrid application (Article 10(3) of Directive No 2001/83/EC), List of Questions adopted on 24.07.2014. 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.

Cyramza (EMEA/H/C/002829), Orphan, (ramucirumab), Applicant: Eli Lilly Nederland B.V., (treatment of gastric cancer)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 23.01.2014.An oral explanation was held on Tuesday 23 September 2014 at 11.00. During the oral explanation the applicant presented the conducted study results and its therapeutic position in treatment of gastric cancer. The applicant explained the patient selection and its impact to treatment outcome. The Committee discussed the studies in relation to the monotherapy indication and the suitable patient subsets. The Committee adopted a positive opinion by majority (24 positive out of 32 votes) recommending the granting of a marketing authorisation together with the CHMP assessment report and translation timetable. Furthermore, the CHMP considered that Ramucirumab is a new active substance, as claimed by the applicant. The Norwegian Member was in agreement with the CHMP recommendation, the Icelandic member did not agree. The CHMP noted the letter of recommendation dated 24.09.2014. The legal status was agreed as medicinal product subject to restricted medical prescription. The divergent position (Pierre Demolis, Sol Ruiz, Concepcion Prieto-Yerro, Hubert Leufkens, Pieter de Graeff, Jan Mazag, Kolbeinn

Gudmundsson, Juris Pokrotnieks, Romaldas Maciulaitis) was appended to the opinion. The summary of opinion was circulated for information. The Committee adopted the BWP Report.

Egranli (EMEA/H/C/002637), (balugrastim), Applicant: Teva Pharma B.V., (treatment of neutropenia)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 22.05.2014. List of Questions adopted on 19.09.2013. 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 balugrastim 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.

Harvoni (EMEA/H/C/003850), (sofosbuvir / ledipasvir), Applicant: Gilead Sciences International Ltd, (treatment of chronic hepatitis C)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Questions adopted on 24.07.2014. 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 ledipasvir 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.

Ketoconazole HRA (EMEA/H/C/003906), Orphan, (ketoconazole), Applicant: Laboratoire HRA Pharma, (treatment of Cushing's syndrome)
Well-established use application (Article 10a of Directive No 2001/83/EC), 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 medical prescription. The summary of opinion was circulated for information. The Communication plan and DHPC letter were agreed by the Committee. The imposed PASS (registry to collect data on the safety profile) was agreed with yearly submissions.

Lymphoseek (EMEA/H/C/002085), (tilmanocept), Applicant: Navidea Biopharmaceuticals Limited, (used in the delineation and localisation of lymph nodes)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 20.03.2014, 19.12.2013, 24.10.2013. List of Questions adopted on 30.05.2013.The CHMP noted the SAG report. The CHMP agreed that no oral explanation was needed at this time. The CHMP discussed the effect of clinical outcome and the heterogeneity of patients. There was also discussion about how to apply the technology and the proposed indication. The CHMP adopted a positive opinion by majority (25 positive out of 32 votes) together with the CHMP Assessment Report. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Andrea Laslop, Concepcion Prieto Yerro, Jan Mazag, Alar Irs, Ivana Mikacic, Kristina Dunder, Sol Ruiz) was appended to the opinion. The summary of opinion was circulated for information.
See also 1.1 Pre-authorisation procedure oral explanations

Moventig (EMEA/H/C/002810), (naloxegol), Applicant: AstraZeneca AB, (treatment of opioid-induced constipation (OIC))
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 23.01.2014. 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 naloxegol 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.

Rezolsta (EMEA/H/C/002819), (darunavir / cobicistat), Applicant: Janssen-Cilag International N.V., (treatment of HIV, immunodeficiency virus (HIV-1) in
- antiretroviral therapy (ART) naïve adults.
- ART-experienced adults with no darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 106/l.)
Fixed combination application (Article 10b of Directive No 2001/83/EC). List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 20.02.2014. 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 Committee noted the letter of recommendations dated 24.09.2014. The summary of opinion was circulated for information.

Tadalafil Mylan (EMEA/H/C/003787), (tadalafil), Applicant: GENERICS (UK) LIMITED, Generic, Generic of Cialis, (treatment of erectile dysfunction)
Generic application (Article 10(1) of Directive No 2001/83/EC), List of Questions adopted on 25.04.2014.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.

Trulicity (EMEA/H/C/002825), (dulaglutide), Applicant: Eli Lilly Nederland B.V., (treatment of type 2 diabetes mellitus)
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 26.06.2014. List of Questions adopted on 20.02.2014. 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 dulaglutide 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. The Committee adopted the BWP Report.

Vargatef (EMEA/H/C/002569), (nintedanib), Applicant: Boehringer Ingelheim International GmbH, (treatment of non-small cell lung cancer (NSCLC))
New active substance (Article 8(3) of Directive No 2001/83/EC), List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.02.2014. 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 nintedanib 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.

2.2. Day 180 List of outstanding issues – New full applications

(EMEA/H/C/003724), Orphan, (eliglustat), Applicant: Genzyme Europe BV, (treatment of Gaucher disease type 1)
List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.02.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable.

(EMEA/H/C/003729), (secukinumab), (treatment of plaque psoriasis)
List of Questions adopted on 20.03.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable. The Committee adopted the BWP Report.

(EMEA/H/C/003773), (cangrelor), (inhibitor indicated for the reduction of thrombotic cardiovascular events
Hemaxiv is a P2Y12 platelet inhibitor indicated for the reduction of thrombotic cardiovascular events (including stent thrombosis) in adult patients with coronary artery disease undergoing percutaneous coronary intervention (PCI). During the pre-operative period when oral P2Y12 therapy is interrupted due to surgery ('Bridging'). Hemaxiv is also indicated to maintain P2Y12 inhibition in adult patients with acute coronary syndromes or in patients with stents who are at increased risk for thrombotic events (such as stent thrombosis) when oral P2Y12 therapy is interrupted due to surgery ('Bridging')). List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable. The CHMP agreed to consult SAG and adopted the list of questions to the experts.

(EMEA/H/C/002066), (ciclosporin), (treatment of keratitis)
List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable. The CHMP agreed to consult an ad-hoc expert group and adopted a List of Questions to the experts.

(EMEA/H/C/002789), Orphan, (levofloxacin), Applicant: Aptalis Pharma SAS, (indicated for chronic pulmonary infections)
List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable. The Committee adopted a List of Question to SAG on Anti-infectives.

(EMEA/H/C/003746), (apremilast), (treatment of psoriatic arthritis, psoriasis)
List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable.

(EMEA/H/C/003771), (nonacog gamma), (treatment of haemophilia B)
List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.03.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted 2nd List of Outstanding Issues with a specific timetable. The Committee adopted the BWP Report.

(EMEA/H/C/002396), (safinamide), (treatment of Parkinson's disease (PD))
List of Questions adopted on 25.04.2014.The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable.

(EMEA/H/C/002840), (dalbavancin), , (treatment of tissue infections (cSSTI))
List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues. The CHMP agreed to the request by the applicant for an extension to the clock stop with a specific timetable.

(EMEA/H/C/002814), (vorapaxar), (indicated for the reduction of atherothrombotic events)
List of Questions adopted on 25.04.2014. The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a List of Outstanding Issues with a specific timetable. The CHMP adopted a list of questions to the SAG CVS.

2.3. Day 120 List of Questions – New full applications

(EMEA/H/C/004006), (clopidogrel), (prevention of myocardial infarction, ischaemic stroke, peripheral arterial disease, acute coronary syndrome, prevention of atherothrombotic and thromboembolic events in atrial fibrillation.)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003837), (dasabuvir), (treatment of chronic hepatitis C)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003725), Orphan, (panobinostat), Applicant: Novartis Pharmaceuticals UK Limited, (treatment of multiple myeloma)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003870), Orphan, (tasimelteon), Applicant: Vanda Pharmaceuticals Ltd., (treatment of Non-24-Hour Sleep-Wake Disorder (Non-24))
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/002839), (sonidegib), (treatment of basal cell carcinoma (BCC))
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003821), Orphan, (nintedanib), Applicant: Boehringer Ingelheim International GmbH (treatment of Idiopathic Pulmonary Fibrosis (IPF))
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003834), Orphan, (idebenone), Applicant: Santhera Pharmaceuticals (Deutschland) GmbH, (treatment of Leber's Hereditary Optic Neuropathy (LHON))
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003971), (sevelamer), (control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003968), (sevelamer), (control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/003839), (ombitasvir / paritaprevir / ritonavir), (treatment of chronic hepatitis C)
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

(EMEA/H/C/002616), Orphan, (pitolisant hydrochloride), Applicant: Bioprojet Pharma, (treatment of narcolepsy)
The Committee discussed 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 new applications for Centralised Procedures

(EMEA/H/C/003759), (guanfacine), (treatment of ADHD)
List of Questions adopted on 24.07.2014. The CHMP agreed to the request by the applicant for an extension to the clock stop.

(EMEA/H/C/003776), (ferric citrate coordination complex), (treatment of hyperphosphataemia)
List of Questions adopted on 24.07.2014. The CHMP agreed to the request by the applicant for an extension to the clock stop.

2.5. Products in the Decision Making Phase

Vantobra (EMEA/H/C/002633) (Tobramycin), Applicant: PARI Pharma GmbH, Hybrid application (Article 10(3) of Directive No 2001/83/EC)

3. Extension of Marketing Authorisation according to Annex I of Regulation 1234/2008

3.1. Extension of marketing authorisation according to Annex I of Regulation 1234/2008; Opinions

Signifor (EMEA/H/C/002052/X/0010), Orphan, (pasireotide), MAH: Novartis Europharm Ltd, Rapporteur: Kristina Dunder, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Qun-Ying Yue, "Line extension application for Signifor to add 20mg, 40mg and 60mg powder and solvent for suspension for injection in the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with other somatostatin analogues." List of Outstanding Issues adopted on 24.07.2014. List of Questions adopted on 20.03.2014. 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.

3.2. Extension of marketing authorisation according to Annex I of Regulation 1234/2008; Day 180 List of outstanding issues

No items

3.3. Extension of marketing authorisation according to Annex I of Regulation 1234/2008; Day 120 List of Questions

Oprymea (EMEA/H/C/000941/X/0017), (pramipexole), MAH: Krka d.d. Novo mesto, Generic, Generic of Sifrol, Rapporteur: Jens Heisterberg, PRAC Rapporteur: Doris Stenver, "To add new strengths 2.62 mg and 3.15 mg prolonged-release tablets." The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Optisulin (EMEA/H/C/000309/X/0079/G), (insulin glargine), MAH: Sanofi-aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Pieter de Graeff, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "To extend MA of Optisulin to register additional strength 300 U/ml, grouped with type IA variation to vary the invented name from Optisulin to Toujeo"
The Committee discussed the issues identified in this application. The Committee adopted the CHMP recommendation and scientific discussion together with the List of Questions.

Somavert (EMEA/H/C/000409/X/0072), (pegvisomant), MAH: Pfizer Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Arnaud Batz, "Addition of 25 mg and 30 mg powder and solvent for solution for injection." The Committee discussed the issues identified in this application.
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 Regulation. 1234/2008

No items

4. Type II variations - Extension of indication procedures

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

Abraxane (EMEA/H/C/000778/II/0067), (paclitaxel), MAH: Celgene Europe Limited, Rapporteur: Pieter de Graeff, Co-Rapporteur: Ingunn Hagen Westgaard, PRAC Rapporteur: Sabine Straus, "Extension of Indication to add a new indication for Abraxane in combination with carboplatin for the first-line treatment of non-small cell lung cancer (NSCLC) in adult patients who are not candidates for potentially curative surgery and/or radiation therapy. Consequently the MAH proposes to update sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmpC and to update the Package Leaflet accordingly. An updated RMP version 14.0 has been provided as part of the application." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Aloxi (EMEA/H/C/000563/II/0038), (palonosetron), MAH: Helsinn Birex Pharmaceuticals Ltd., Rapporteur: Patrick Salmon, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Almath Spooner, "Extension of the therapeutic indication for paediatric patients 1 month of age and older for the prevention of nausea and vomiting associated with moderately and highly emetogenic cancer chemotherapy for the IV formulation, based on the paediatric studies PALO-10-14 and PALO-10-20 and update of sections 5.1 and 5.2 of the Aloxi Oral formulation to reflect those studies. The MAH took the opportunity of this variation to update the Aloxi product information annexes in line with Version 9 of the QRD template." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Avastin (EMEA/H/C/000582/II/0072), (bevacizumab), MAH: Roche Registration Ltd, Rapporteur: Jens Ersbøll, Co-Rapporteur: Ingunn Hagen Westgaard, PRAC Rapporteur: Doris Stenver, "Extension of indication for the use of Avastin in combination with paclitaxel and cisplatin or paclitaxel and topotecan in patient with persistent, recurrent, or metastatic carcinoma of the cervix. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC and the Package Leaflet are proposed to be updated." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Eylea (EMEA/H/C/002392/II/0013), (aflibercept), MAH: Bayer Pharma AG, Rapporteur: Pierre Demolis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Arnaud Batz, "Update of the Product information to introduce new indication: the treatment of macular oedema following branch retinal vein occlusion (BRVO). New clinical and nonclinical data is being introduced to the SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2. The PL is being updated accordingly. Furthermore, minor editorial changes have been introduced to the PI." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Jakavi (EMEA/H/C/002464/II/0016), Orphan, (ruxolitinib), MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to add treatment of adult patients with polycythaemia vera resistant to or intolerant of hydroxyurea. As a result, the MAH proposes to update sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC. The Package Leaflet is proposed to be updated accordingly. In addition, the MAH took the opportunity to implement imnor editorial changes in the SmPC. An updated RMP version 4.0 has been provided as part of the application." The Committee discussed the

issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Javlor (EMEA/H/C/000983/II/0011), (vinflunine ditartrate), MAH: Pierre Fabre Médicament, Rapporteur: Greg Markey, Co-Rapporteur: Arantxa Sancho-Lopez, PRAC Rapporteur: Julie Williams, "Extension of Indication: in combination with capecitabine for the treatment of adult patients with locally advanced or metastatic breast cancer not amenable to curative surgery or radiotherapy, who are capecitabine and vinca alkaloid naïve, and were previously treated with or resistant to an anthracycline and who are taxane resistant." Request for Supplementary Information adopted on 25.04.2014, 19.09.2013. Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004). An oral explanation was held on Tuesday 23 September 2014 at 9.00. See also 1.3 Post-authorisation procedure oral explanations. During the oral explanation the applicant presented the efficacy results and tolerability. The Committee raised questions about the clinical effectiveness. The CHMP 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 EMA question and answer document was circulated for information.

Prezista (EMEA/H/C/000707/II/0063), (darunavir), MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus, "Update of section 4.1 of the SmPC for the 100mg/ml oral suspension and the 400mg, 800mg film-coated tablets with information on the use of darunavir with cobicistat as pharmacokinetic enhancer. Consequential changes have been introduced in the SmPC and the PL of all formulations. Update of the Annex II with a correction to the address of one of the manufacturers responsible for batch release. Update of the PL with the local representatives' contact information for France, Romania, Ireland and Cyprus." Request for Supplementary Information adopted on 26.06.2014, 25.04.2014. 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 and translation timetable. The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations. The summary of opinion was circulated for information.

Prezista (EMEA/H/C/000707/II/0064), (darunavir), MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Sabine Straus, "Update of the SmPC with an extension of indication in treatment naïve children aged 3 to 12 years and changes in the posology of the treatment experienced children aged 3 to 12 years with no DRV RAMs based on the data from a 2 week qd substudy of the Phase 2 study TMC114 C228 and results from model-based pharmacokinetic simulations. The PL has been updated accordingly." Request for Supplementary Information adopted on 22.05.2014. 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 and translation timetable. The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations. The summary of opinion was circulated for information.

Travatan (EMEA/H/C/000390/II/0046), (travoprost), MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas, "Extension of the therapeutic indication for decrease of elevated intraocular pressure in paediatric patients with ocular hypertension or paediatric glaucoma." The Committee

discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Tresiba (EMEA/H/C/002498/II/0011), (insulin degludec), MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Extension of the indication in children aged from 1 to 18 years. Update to sections 4.1, 4.2, 4.8 and 5.1 of the SmPC. The PL is updated accordingly. In addition, update of the Section 2 of the PL in line with the existing information in Section 4.2 of the SmPC." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Velcade (EMEA/H/C/000539/II/0072), (bortezomib), MAH: Janssen-Cilag International N.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Carmela Macchiarulo, "Extension of indication for the use of VELCADE in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for the treatment of adult patients with previously untreated mantle cell lymphoma. Consequently, the MAH proposed updates of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC and the Package Leaflet." The Committee discussed the issues identified in this application. The Committee adopted a Request for Supplementary Information with a specific timetable.

Xagrid (EMEA/H/C/000480/II/0059), Orphan, (anagrelide), MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Pierre Demolis, Co-Rapporteur: Daniel Brasseur "Update of the SmPC in order to add information on the study results from study SPD422-405 and SPD422-404. As a consequence, update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the efficacy and safety information of anagrelide in the paediatric population. A warning on the risk of progression to AML and myelofibrosis and monitoring of signs and symptoms of disease progression have also been highlighted. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 24.07.2014, 22.05.2014. 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 and translation timetable. The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

Xiapex (EMEA/H/C/002048/II/0044), (collagenase clostridium histolyticum), MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Martin Huber, "Update of the SmPC with a new indication in the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity. The PL is updated accordingly." 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 Committee adopted a Request for Supplementary Information with a specific timetable.

4.2. Update on on-going Type II variation - Extension of indications

No items

5. Ancillary medicinal substances in medical devices

5.1. Opinions / List of outstanding issues / List of Questions

(EMEA/H/D/002769), (thrombin), (is indicated in surgical procedures)
Ancillary medicinal substance/blood derivative substance (Article 1(4)/1(4a) of both Directives No 93/42/EEC and 90/385/EEC). List of Outstanding Issues adopted on 26.06.2014, 25.04.2014.
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.

Floseal Hemostatic Matrix (Floseal VH S/D) (EMEA/H/D/000956/X/0016), (human thrombin), Applicant: TÜV SÜD Product Service GmbH, "Addition of a new strenght/concentration: 5000 IU Thrombin/vial (500 IU Thrombin/mL)." List of Questions adopted on 22.05.2014. 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 and translation timetable. The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations. The summary of opinion was circulated for information.

(EMEA/H/D/003740), (human serum albumin), (the storage, manipulation, in-vitro culture and transfer of human gametes)
List of Questions adopted on 23.01.2014. The CHMP adopted a List of Outstanding Issues with a specific timetable. The Committee adopted the BWP Report.

(EMEA/H/D/002831), ((substance to be reviewed) insulin-like growth factor-i (igf-i) segment), (hard-to-heal wounds, primarily venous leg ulcers), List of Questions adopted on 23.01.2014.
The CHMP adopted the List of Outstanding Issues with a specific timetable.
The Committee adopted the BWP Report.

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

No items

7. Re-examination procedure (type II variations) under Article 6(9) of Commission Regulation EC No 1085/2003

Avastin (EMEA/H/C/000582/II/0059), (bevacizumab), MAH: Roche Registration Ltd "Extension of indication to include Avastin in combination with radiotherapy and temozolomide for the treatment of adult patients with newly diagnosed glioblastoma." Opinion adopted on 22.05.2014. Request for Supplementary Information adopted on 21.11.2013, 27.06.2013. An oral explanation was held on Monday 22 September 2014 at 14.00. During the oral explanation the applicant addressed the main methodological issues related to clinical benefit. The Committee discussed the issues related to clinical benefit further. The Committee adopted a negative opinion by majority (19 negative out of 30

votes) together with the assessment report. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Agnes Gyurasics, Jan Mueller-Berghaus, Mila Vlaskovska, Jens Heisterberg, Outi Maki-Ikola, Panayiotis Triantafyllis, Juris Pokrotnieks, Dimitrios Kouvelas, David Lyons, Harald Enzmann, John Joseph Borg) was appended to the opinion. The EMA question and answer document was circulated for information. See also 1.2 Re-examination procedure oral explanation.

8. Withdrawal of application

No items

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

No items

10. Pre-submission issues

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

11. Post-authorisation issues

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

Valdoxan, Thymanax (EMEA/H/C/000916/PSUV/0021, EMEA/H/C/000915/PSUV/0023) (Agomelatine), MAH: Servier (Ireland) Industries Ltd., Rapporteur: Karsten Bruins Slot, Co-Rapporteur: Filip Josephson. The members were reminded of previous discussions and the remaining issues. The members discussed the PRAC recommendation about the contraindication, that the medicine should not be used in patients aged 75 years or over. The members noted the DHPC letter, but did not support it. CHMP adopted the patient information and SmPC. The CHMP adopted a final opinion by majority (26 out of 32 votes) recommending the variation to the terms of the Marketing Authorisation. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Robert Hemmings, Sol Ruiz, Jens Heisterberg, Concepcion Prieto-Yerro, Ivana Mikacic, Greg Markey) was appended to the opinion. The CHMP agreed to the wording of the public health communication.

M-M-RVAXPRO (EMEA/H/C/000604/II/0063), (measles, mumps and rubella vaccine (live)), MAH: Sanofi Pasteur MSD SNC, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to include "Transverse myelitis". The CHMP adopted a request for supplementary information with a specific timetable.

12. Referral Procedures

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

MACI (EMEA/H/A20/1409/C/002522/0004)

(Matrix Applied Characterised Autologous Cultured Chondrocytes), MAH: Aastrom Biosciences DK ApS, Rapporteur: Elaine French, Co-Rapporteur: Johannes H. Ovelgönne, CHMP Co-ordinators: Greg Markey, Johann Lodewijk Hillege, (repair of symptomatic cartilage defects of the knee), New active substance (Article 8(3) of Directive No 2001/83/EC)

The members noted the letter from the European Commission dated 10 September 2014 notifying of a referral under Article 20. The CHMP was informed of the draft opinion prepared by the CAT recommending to suspend the marketing authorisation for MACI. The Committee adopted by consensus an opinion, based on the draft opinion prepared by the CAT recommending the suspension of the marketing authorisation, together with the CHMP Assessment Report. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The Committee noted the wording of the public health communication.

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

Medicinal products under development for the treatment of Ebola (EMEA/H/A-5(3)/1410)

The CHMP noted the letter from the EMA dated 23 September 2014 notifying of a request for a CHMP opinion under Article 5(3).

The CHMP adopted a List of Questions with a specific timetable.

Start of procedure: September 2014 CHMP

List of Questions: 25.09.2014

Submission of responses by: 10.10.2014

Co-Rapporteurs' assessment reports circulated to CHMP: 28.10.2014

Rapporteur's overall assessment report circulated to CHMP: 06.11.2014

Comments: 12.11.2014

CHMP discussion: November 2014 CHMP

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

No items

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

No items

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

EMLA Cream (EMEA/H/A-30/1388) (lidocaine / prilocaine), Astra Zeneca group of companies and associated companies, Rapporteur: Martina Weise, Co-Rapporteur: Greg Markey.
Harmonisation exercise for EMLA Cream. The review was triggered by Germany, due to the need of harmonisation of the Summary of Product Characteristics across Member States. List of Outstanding Issues adopted on 22.05.2014, 24.07.2014. List of Questions adopted in October 2013. Extension of Timetable adopted in November 2013. The CHMP agreed that all outstanding issues were considered resolved. The CHMP adopted an opinion by consensus, recommending the variation to the terms of the Marketing Authorisations. The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The question-and-answer document was circulated for information.

Nasonex (EMEA/H/A-30/1374) (mometasone), nasal spray suspension, MAH: Merck Sharp & Dohme, Rapporteur: Kristina Dunder, Co-Rapporteur: David Lyons.
Nasonex was included in the list of products for SmPC harmonisation, drawn up by the CMDh, in accordance with Article 30(2) of Directive 2001/83/EC. The CHMP adopted a 2nd List of Outstanding Issues to the MAH with a specific timetable.
Responses: 3 October 2014, Restart of the procedure: 6 October 2014, Joint or Rapporteurs Assessment report(s): 10 October 2014, Comments from CHMP members: 15 October 2014, List of outstanding issues and/or Oral explanation and/or CHMP opinion: October 2014 CHMP

Ikorel / Dancor and associated names (EMEA/H/A-30/1380) (nicorandil), Sanofi-Aventis group of companies and associated companies / Merck group of companies and associated companies, Rapporteur: Pierre Demolis, Co-Rapporteur: Pieter de Graeff.
Ikorel / Dancor was included in the list of products for SmPC harmonisation, drawn up by the CMDh, in accordance with Article 30(2) of Directive 2001/83/EC. The CHMP adopted a List of outstanding issues with a specific timetable.
Responses: 01 December 2014; Restart of the procedure: 23 December 2014; Joint assessment report circulated to CHMP: 07 January 2015; Comments: 12 January 2015; List of outstanding issues or CHMP opinion: January 2015 CHMP

Cymevene IV and associated names (EMEA/H/A-30/1406) (ganciclovir), F. Hoffmann-La Roche, Rapporteur: Rugile Pivliene, Co-Rapporteur: Alar Irs. The CHMP noted the Letter from the European Commission notifying of a referral under Article 30. The Rapporteur changed from Romaldas Maciulaitis to Rugile Pivliene. The CHMP adopted a List of Questions with a specific timetable.
Responses: 5 January 2015; Restart of the procedure: 27 January 2015; Joint assessment reports circulated to CHMP: 11 February 2015; Comments: 16 February 2015 ; List of outstanding issues or CHMP opinion: February 2015 CHMP

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

Adrenaline auto injectors (EMEA/H/A-31/1398), Rapporteur: Alars Irs, Co-Rapporteur: Robert Hemmings. Article 31 triggered by the MHRA due to the lack of robust evidence that the devices deliver the adrenaline intramuscularly in all patients. The CHMP agreed to consult an ad-hoc expert group. The CHMP adopted a List or Questions to an ad-hoc expert group as well as to Healthcare Professionals' Organisations. The CHMP adopted a List of Outstanding Issues with a specific timetable.

Responses: 18 December 2014; Ad hoc expert group meeting: January 2015 (date to be confirmed); Restart of the procedure: 27 January 2015; Joint assessment report circulated to CHMP: 09 February 2015; Comments: 16 February 2015; List of outstanding issues or CHMP opinion: February 2015 CHMP

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097)
Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff. The CHMP adopted the Assessment Reports of the 4th annual cumulative review submissions.

GVK Bio (EMEA/H/A-31/1408) Article 31 procedure triggered by the European Commission concerning GVK Biosciences Private Limited (GVK Bio), Swarna Jayanthi commercial complex, Ameerpet, Hyderabad 500 038, India. The CHMP noted the letter from the European Commission dated 1 August 2014 informing of an official referral under Article 31 and its grounds. The CHMP appointed Harald Enzmann as lead Rapporteur and Christian Schneider as Co-Rapporteur. The CHMP adopted a List of questions to the CRO with a specific timetable.
Responses: 03.10.2013; Rapporteur and co-rapporteur' assessment reports circulated to CHMP: 13.10.2013; Comments: 15.10.2013; Updated rapporteur and co-rapporteur' assessment reports circulated to CHMP: 16.10.2013; List of outstanding issues/ possible oral explanation: October 2014 CHMP

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

No items

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

Ketoprofen formulation for topical use (EMEA/H/A-107/1259)
(Ketum), Rapporteur: Joseph Emmerich, Co-Rapporteur: Radka Montoniová,
Assessment of MAHs' responses to the list of questions adopted in March 2014 concerning the Surveillance study of photo-contact dermatitis leading to hospitalisation in Europe with a special focus on topical ketoprofen and other topical NSAIDs, including evaluation of severe photosensitivity reactions (PASS pilot study) and the 3-years cumulative analysis of photosensitivity reactions including photo-allergy reactions together with a report of the effectiveness of risks minimisation measures. The CHMP adopted the Rapporteurs' Assessment report concluding that a nationally-tailored approach to the need for DHPCs and/or other communications is a way forward to maintain awareness of prescribers and that no further co-ordinated regulatory action between Marketing Authorisation Holders and the CHMP is needed any longer on this issue. A letter to the concerned MAHs will be sent by EMA.

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

No items

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

No items

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 items

13. Pharmacovigilance issues

Summary of recommendations and advice of PRAC meeting held on 8-11 September 2014: **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 September 2014: **For adoption**	The EURD list was adopted.
Early Notification System: September 2014 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 ITF: 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. Eligibility to EMA scientific services

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

Request from EDQM for EMA scientific Opinion under Art. 57 (1)P of Regulation (EC) No 726/2004 • Draft Report: **For discussion**	The CHMP noted the draft report.

15.5. Nanomedicines activities

16. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 1-4 September 2014 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

SAG Neurology meeting on 3 October on valproate and related substances, on request from PRAC • List of experts: **For adoption**	The CHMP adopted the list of experts.
SAG CVS meeting on 30 September on ivabradine, on request from PRAC • List of experts: **For adoption**	The CHMP adopted the list of experts.

Inter-Committee SAG Oncology meeting on 10 October on ONJ associated with bisphosphonates and denosumab, on request from PRAC • List of experts: **For adoption** • List of Questions: **For adoption**	The CHMP adopted the list of experts and the list of questions to this group.

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 22-24 September 2014: **For information**	The CHMP noted the report.
CMDh request for advice from QWP regarding the droplet size distribution for a nasal spray: **For discussion**	The CHMP agreed to the CMDh request for advice from QWP.
Question on the clinical impact of differences in the Dv10 and Dv90 values of the droplet size distribution: **For information**	The CHMP noted the question.

18. Other Committees

18.1. Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 3-4 September 2014: **For information**	To be sent in the Post-mail.

18.2. Committee for Herbal Medicinal Products (HMPC)

Not applicable.

18.3. Paediatric Committee (PDCO)

PIPs reaching D30 at September 2014 PDCO: **For information**	To be sent in the Post-mail.
Report from the PDCO meeting held on held on 10-12 September 2014: **For information**	The CHMP noted the report.

18.4. Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 18-19 September 2014: **For information**	The CHMP noted the Table of Decisions.

19. Invented name issues

Table of Decisions of the NRG Table of Decisions of the NRG accelerated review procedure performed in August 2014: **For adoption**	The CHMP adopted the NRG Table of Decisions.

20. Any other business

Area of expertise of Co-opted Member in light of Jan Mueller –Berghaus' mandate expiring in November 2014 Area of expertise: **For agreement**	The CHMP agreed on the area of expertise: Quality and safety of biological medicinal products, including biotechnology derived medicines, cell therapy and gene therapy.
CAT - expiry of mandates of CHMP representatives: **For discussion**	The CHMP should be reminded of the upcoming expiry of mandates of the CHMP representatives and/or their alternates in the CAT. Current members are: Sol Ruiz, Romaldas Maciulaitis, Bruno Sepodes, John Borg, Jean-Louis Robert.
CHMP Work Plan 2015: **For information**	Postponed.
Procedural Advice on the CHMP/CAT/PRAC (Co)Rapporteur appointment: **For adoption**	The CHMP adopted the procedural advice document which had been updated following comments from the PRAC.
Concept paper on the need for revision of the points to consider on the clinical investigation of new medicinal products for the treatment of acute coronary syndrome (CPMP/EWP/570/98 and CPMP/EWP/967/01) (EMA/559636/2014): **For adoption and release for 3 months public consultation**	The CHMP adopted the concept paper for release for 3-months public consultation.
Request for nomination of Vice Chair for Central Nervous System Working Party The new vice-chair will be determined by the CHMP based on their expertise in neurology and psychiatry as well as experience within the European regulatory network in October 2014.	
Q3D Guideline for Elemental Impurities: **For discussion**	The CHMP discussed the proposed timeline of 36 months of implementation of Q3D for already marketed products not new applications in the EU.
Election of Vice-Chair of Pharmacogenomics Working Party	The CHMP elected Markus Paulmichl as Vice-chair of the Pharmacogenomics Working Party.
Election of Vice-Chair of Biostatistics Working Party	The CHMP elected Thomas Lang as Vice-Chair of the Biostatistics Working Party.

Election of Vice-Chair of Pharmacokinetics Working Party	The CHMP elected Alfredo García-Arieta as Vice-chair of the Pharmacokinetics Working Party.
Nomination of new observer to the SAWP: **For adoption**	The CHMP endorsed Ira Palminger Hallen as new observer to the SAWP.
Status update on proposed process improvements for initial MAA	The CHMP noted the status update on proposed process improvements for initial MAA and agreed to the principles.
IQ Consortium Induction Working Group - Questions for Discussion/Feedback (16 September 2014): **For adoption**	The CHMP adopted the questions.
PKWP agenda for the meeting 21-22 October 2014: **For information**	Noted.
Quarterly report of initial MAAs submissions with appointed Rapporteurs: **For information**	Noted.
Agenda of CHMP, CAT, COMP joint Strategic meeting under the Italian EU presidency, 29-30 October 2014	The CHMP noted the agenda of the CMP, CAT, COMP joint strategic meeting.

21. List of participants: including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 22-25 September 2014 meeting.

CHMP Chair	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which restrictions applies Product / substance
Tomas Salmonson	Sweden	Full involvement	

CHMP Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which restrictions applies Product / substance
Andrea Laslop	Austria	Full involvement	
Daniel Brasseur	Belgium	Full involvement	
Mila Vlaskovska	Bulgaria	Full involvement	
Ivana Mikačić	Croatia	No participation in final deliberations and voting	(EMEA/H/C/002840)
Panayiotis Triantafyllis	Cyprus	Full involvement	
Ondřej Slanař	Czech Republic	No participation in discussions, final deliberations and voting	(EMEA/H/C/003837)
			(EMEA/H/C/003839)
			Rezolsta (EMEA/H/C/002819)
			Optisulin (EMEA/H/C/000309/X/0079/G)
			Tresiba (EMEA/H/C/002498/II/0011), (insulin degludec)
			Travatan (EMEA/H/C/000390/II/0046)
			(travoprost) (EMEA/H/C/002840)
		No participation in final deliberations and voting	Brimica Genuair (EMEA/H/C/003969)
			Duaklir Genuair (EMEA/H/C/003745)
			Budesonide/Formoterol Teva (EMEA/H/C/003951)
			Vylaer Spiromax (EMEA/H/C/003952)
			(EMEA/H/C/003729)
			(EMEA/H/C/003746)
Jens Heisterberg	Denmark	Full involvement	
Alar Irs	Estonia	Full involvement	
Outi Mäki-Ikola	Finland	No participation in final deliberations and voting	(EMEA/H/C/003729)
			(EMEA/H/C/003746)

CHMP Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which restrictions applies Product/substance
			(EMEA/H/C/003971) (EMEA/H/C/003968)
Pierre Demolis	France	Full involvement	
Harald Enzmann	Germany	Full involvement	
Dimitrios Kouvelas	Greece	Full involvement	
Agnes Gyurasics	Hungary	Full involvement	
Kolbeinn Gudmundsson	Iceland	Full involvement	
David Lyons	Ireland	Full involvement	
Daniela Melchiorri	Italy	Full involvement	
Juris Pokrotnieks	Latvia	Full involvement	
Romaldas Mačiulaitis	Lithuania	Full involvement	
Jacqueline Genoux-Hames	Luxembourg	Full involvement	
John Joseph Borg	Malta	Full involvement	
Pieter de Graeff	Netherlands	Full involvement	
Karsten Bruins Slot	Norway	Full involvement	
Piotr Fiedor	Poland	Full involvement	
Bruno Sepodes	Portugal	Full involvement	
Jan Mazag	Slovakia	Full involvement	
Stanislav Primožič	Slovenia	Full involvement	
Concepcion Prieto Yerro	Spain	Full involvement	
Kristina Dunder	Sweden	Full involvement	
Greg Markey	United Kingdom	Full involvement	
Robert James Hemmings	Co-opted	Full involvement	
Hubert Leufkens	Co-opted	Full involvement	
Jan Mueller-Berghaus	Co-opted	Full involvement	
Jean-Louis Robert	Co-opted	Full involvement	
Sol Ruiz	Co-opted	Full involvement	

CHMP Alternate	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which restrictions applies Product / substance
Milena Stain	Austria	Full involvement	
Bart Van der Schueren	Belgium	Full involvement	
Ana Dugonjić	Croatia	Full involvement	
Radka Montoniová	Czech Republic	Full involvement	
Christian Schneider	Denmark	Full involvement	also via TC on Monday 22.09.2014
Janne Komi	Finland	Full involvement	
Joseph Emmerich	France	No participation in final deliberations and voting	EMLA Cream (EMEA/H/A-30/1388) (EMEA/H/C/004006) (EMEA/H/C/003773) (EMEA/H/C/002814)
Martina Weise	Germany	Full involvement	
George Aislaitner	Greece	Full involvement	
Melinda Sobor	Hungary	Full involvement	
Patrick Salmon	Ireland	Full involvement	
Johann Lodewijk Hillege	Netherlands	Full involvement	
Ingunn Hagen Westgaard	Norway	Full involvement	
Aldona Paluchowska	Poland	Full involvement	
Dinah Duarte	Portugal	Full involvement	
Dana Gabriela Marin	Romania	Full involvement	*Replacing CHMP member*
Arantxa Sancho-Lopez	Spain	Full involvement	
Filip Josephson	Sweden	Full involvement	
Rafe Suvarna	United Kingdom	Full involvement	

European Commission	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which restriction applies Product / substance
	European Commission	Full involvement	
	European Commission	Full involvement	
	European Commission	Full involvement	

CHMP Expert	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which the expert is invited Product/substance
* Experts were only evaluated against the product they have been invited to talk about.			
Christophe Focke	Belgium	Full involvement	
Jana Lukacisinova	Czech Republic	Full involvement	
Mette Tranholm	Denmark	Full involvement	
Nicolas Antih	France	Full involvement	
Catherine Deguines	France	Full involvement	
Khodor Chatila	France	Full involvement	
Sabine Mayrhofer	Germany	Full involvement	
Jens Bäte	Germany	Full involvement	
Ralf Meyer	Germany	Full involvement	
Ivana Pankuchova	Slovakia	Full involvement	
Ana Alonso Gutierrez	Spain	Full involvement	
Elina Rönnemaa	Sweden	Full involvement	
Anna Lundberg	Sweden	Full involvement	
Bertil Johnson	Sweden	Full involvement	
Marie Bielsky	United Kingdom	Full involvement	
Emmanouil Zouridakis	United Kingdom	Full involvement	
Yolanda Barbachano	United Kingdom	Full involvement	
James Swales	United Kingdom	Full involvement	
Bronwyn Grimshaw	United Kingdom	Full involvement	
David Silverman	United Kingdom	Full involvement	
June Munro Raine	United Kingdom	Full involvement	
Jasmin Barman-Aksozen	Switzerland	Full involvement	Patient
Francois Houyez	France	Full involvement	Patients' mentor
Geoffrey Sloan	United Kingdom	Full involvement	Patient

CHMP Expert by phone	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the September 2014 Minutes for which the expert is invited Product/substance
* Experts were only evaluated against the product they have been invited to talk about.			
Beate Ziegeler	Germany	Full involvement	
Martin Huber	Germany	Full involvement	
Kristina Bech Jensen	Denmark	Full involvement	
Jan Schellens	Netherlands	Full involvement	
Jens Ersbøll	Denmark	Full involvement	
Sinan B. Sarac	Denmark	Full involvement	
Elisabeth Penninga	Denmark	Full involvement	
Olga Kholmanskikh Van Criekingen	Belgium	Full involvement	
Jorge Camarero Jiménez	Spain	Full involvement	
Qun-Ying Yue	Sweden	Full involvement	
Mair Powell	United Kingdom	Full involvement	
Mirza Catibusic	Ireland	Full involvement	
Amarilla Veres	Hungary	Full involvement	
Ingebjørg Buajordet	Norway	Full involvement	
Helgi Helgason	Iceland	Full involvement	

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)*

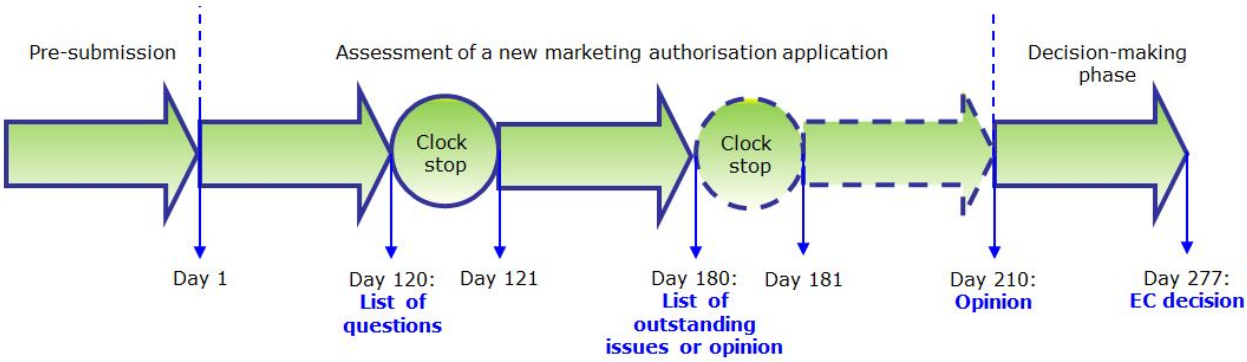
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section 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) No 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.