19 May 2014
EMA/CHMP/252366/2014 Rev. 1

Committee for medicinal products for human use (CHMP)

Agenda of May 2014 meeting

Chair: Tomas Salmonson – Vice-chair: Pierre Demolis

19 May 2014, 13:00 – 19:30, room 3A

20 May 2014, 08:30 – 19:30, room 3A

21 May 2014, 08:30 – 19:30, room 3A

22 May 2014, 08:30 – 16:00, room 3A

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 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

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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.

For adoption

AGENDA (EMA/CHMP/252366/2014) and Annex to CHMP agenda of the CHMP plenary session to be held 19-22 May 2014	
TIMESCHEDULE of the CHMP plenary session to be held 19-22 May 2014	
MINUTES of the CHMP plenary session held 22-25 April 2014 (EMA/CHMP/240831/2014)	
MINUTES of the May 2014 CHMP ORGAM meeting held on 12 May 2014 (EMA/CHMP/287131/2014)	

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 19-22 May 2014.	*See May 2014 minutes (to be published post June 2014 CHMP meeting)*
Draft Agenda of 23-26 June 2014 CHMP plenary	

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(EMEA/H/C/002705), (mixture of polynuclear iron(iii)-oxyhydroxide, sucrose and starches), (indicated for the control of serum phosphorus levels in patients with end-stage renal disease (ESRD)) List of Outstanding Issues adopted in October 2013. List of Questions adopted in May 2013.	Possible Oral explanation to be held on Tuesday 20 May 2014 at 16.00.

(EMEA/H/C/002633), Orphan, (tobramycin), Applicant: PARI Pharma GmbH, (treatment of chronic pulmonary infection) List of Outstanding Issues adopted in October 2013, March, April 2014. List of Questions adopted in February 2013.	Possible Oral explanation to be held on Wednesday 21 May 2014 at 9.00.

1.2. Re-examination Procedure Oral Explanation

Masiviera (EMEA/H/C/002659), Orphan, (masitinib), Applicant: AB Science, (treatment of non resectable locally advanced or metastatic pancreatic cancer) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Report from SAG Oncology held on 7 May 2014: **For discussion**	Possible Oral explanation to be held on Wednesday 21 May 2014 at 11.00. See 6 Re-examination procedure (new applications) under Article 9(2) of Regulation No 726/2004
Nerventra (EMEA/H/C/002546), (laquinimod), Applicant: Teva Pharma GmbH, (treatment of multiple sclerosis) New active substance (Article 8(3) of Directive No 2001/83/EC) Negative Opinion adopted in January 2014. • Report by Serge Bakchine from SAG Neurology meeting held on 8 May 2014: **For discussion**	Possible Oral explanation to be held on Monday 19 May 2014 at 15.00. See also 6 Re-examination procedure (new applications) under Article 9(2) of Regulation No 726/2004
Reasanz (EMEA/H/C/002817) (serelaxin), Applicant: Novartis Europharm Ltd, (treatment of acute heart failure) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Report from SAG CVS held on 12 May 2014: **For discussion**	Possible Oral explanation to be held on Tuesday 20 May 2014 at 14.00. See also 6 Re-examination procedure (new applications) under Article 9(2) of Regulation No 726/2004
Translarna (EMEA/H/C/002720), Orphan, (ataluren), Applicant: PTC Therapeutics Limited, (treatment of Duchenne muscular dystrophy) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014.	Possible Oral explanation to be held on Tuesday 20 May 2014 at 11.00. See also 6 Re-examination procedure (new applications) under Article 9(2) of Regulation No 726/2004

1.3. Post-authorisation Procedure Oral explanation

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Masiviera (EMEA/H/C/002659), Orphan, (masitinib), Applicant: AB Science, (treatment of non resectable locally advanced or metastatic pancreatic cancer) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Report from SAG Oncology held on 7 May 2014: **For discussion** • Opinion: **For adoption**	See also 1.2 Re-examination Procedure Oral Explanation
Nerventra (EMEA/H/C/002546), (laquinimod), Applicant: Teva Pharma GmbH, (treatment of multiple sclerosis) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Report from SAG Neurology meeting held on 8 May 2014: **For discussion** • SWP Report: **For adoption** • Opinion: **For adoption**	See 1.2 Re-examination Procedure Oral Explanation
Reasanz (EMEA/H/C/002817), (serelaxin), Applicant: Novartis Europharm Ltd, (treatment of acute heart failure) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Report from SAG CVS held on 12 May 2014: **For discussion** • Opinion: **For adoption**	See 1.2 Re-examination Procedure Oral Explanation

Translarna (EMEA/H/C/002720), Orphan, (ataluren), Applicant: PTC Therapeutics Limited, (treatment of Duchenne muscular dystrophy) New active substance (Article 8(3) of Directive No 2001/83/EC) Opinion adopted in January 2014. • Letter from 3rd party and scientific report "Benefit-Risk Assessments in Rare Disorders" submitted to the CHMP: **For discussion** • Opinion: **For adoption**	See 1.2 Re-examination Procedure Oral Explanation

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(sitagliptin / metformin hydrochloride), MAH: Merck Sharp & Dohme Limited, Rapporteur: Pieter de Graeff, "Proposal to update section 5.1 of the SmPC with the results of study PN260 which examined the insulin-sparing effect of sitagliptin 100 mg once-daily compared with placebo over 24 weeks in participants with type 2 diabetes mellitus who have inadequate glycaemic control on insulin alone or in combination with metformin."

- Request for Supplementary information / Opinion: **For adoption**

12. REFERRAL PROCEDURES

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

Procoralan (EMEA/H/C/000597)
Corlentor (EMEA/H/C/000598)
Procedure number:
EMEA/H/A20/1404/C/000597-598/0031-0032
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12.2. Requests for CHMP Opinion under Article 5(3) and 57 (1)p of Regulation (EC) No 726/2004

Polymyxin-based products (EMEA/H/A-5(3)/1384) (colistin, colistimethate), Rapporteur: Robert Hemmings, Co-Rapporteur: Martina Weise, Review of the module 3 (quality) and the Eur. Pharm. monograph. Triggered by the EMA Executive Director • Proposal to consult the MSWG (Modelling and simulation working group) on the adequacy of the PK data submitted by the MAH in the context of the on-going procedure: **For adoption**	See also section 12.6 Community Interests - Referral under Article 31

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

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12.4. Disagreement between Member States on application for medicinal product (Potential serious risk to Public Health) –under Article 29(4) of 2001/83/EC

Dexamed 5 mg Tablets (EMEA/H/A-29/1375) (dexamfetamine sulphate film coated tablets), Kohne Pharma GmbH, Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege, Article 29(4) procedure triggered by the Netherlands on the following grounds: enhanced risk for dependence and abuse potential of this product compared to other treatment options in ADHD and lack of convincing evidence for the efficacy in a second line setting – film coated tablets. List of Outstanding Issues adopted in March 2014 by written procedure. • Report from SAG Psychiatry held on 12 May 2014: **For discussion** • Opinion: **For adoption**	Oral explanation to be held on Tuesday 20 May 2014 at 9.00. See also 1.4 Referral Oral explanations

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

EMLA Crème (EMEA/H/A-30/1388)
(lidocaine / prilocaine), Astra Zeneca group of companies and associated companies, Rapporteur: Martina Weise, Co-Rapporteur: Greg Markey

List of Questions adopted in October 2013, Extension of Timetable adopted in November 2013.

- List of Outstanding issues: **For adoption**

Seroquel IR&XR (EMA/H/A-30/1362)
(quetiapine), Astra Zeneca, Rapporteur: Hans Hillege, Co-Rapporteur: Melinda Sobor

List of Outstanding Issues adopted in November 2014. List of Questions adopted in June 2013.

- Opinion: **For adoption**

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

Emergency contraceptives (EMEA/H/A-31/1391)
NAPs:
emergency contraceptive medicinal products containing levonorgestrel and ulipristal

CAP:

ellaOne (ulipristal acetate), MAH: Laboratoire HRA Pharma, SA

Rapporteur: Kristina Dunder, Co-Rapporteur: Pieter de Graeff

Influence of body weight and Body mass index (BMI) of women on the efficacy of the emergency contraceptives. List of Questions adopted in January 2014.

- List of outstanding issues: **For adoption**

Gadolinium containing contrast agents, Gd-Cas (EMEA/H/A-31/1097) Rapporteur: Rafe Suvarna, Co-Rapporteur: Pieter de Graeff, • FUM related to the 3rd annual cumulative safety reviews on nephrogenic systemic fibrosis (NSF): Omniscan (GE HealthCare) fourth monthly update and interim analysis report submission as requested by CHMP in November 2013 and assessment report: **For adoption**	
RAS-acting agents (EMEA/H/A-31/1370) Overall CHMP Rapporteur: Daniela Melchiorri, Overall PRAC Rapporteur: Carmela Macchiarulo (IT), PRAC Co-Rapporteurs: Margarida Guimarães (PT), Valerie Strassmann (DE), Tatiana Magálová (SK), Dolores Montero Corominas (ES), Almath Spooner (IE), Menno van der Elst (NL), Julie Williams (UK), Qun-Ying Yue (SE) Review of the benefit-risk of dual blockade of the renin angiotensin system through concomitant use of ARBs, ACE-inhibitors or aliskiren-containing medicines following the notification by Italy of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data • Opinion: **For adoption** • PRAC recommendation: **For information**	
Polymyxin-based products (EMEA/H/A-31/1383) (colistin, colistimethate), Rapporteur: Robert Hemmings, Co-Rapporteur: Joseph Emmerich, Full benefit-risk review and update and harmonisation of the product information. Triggered by European Commission • Proposal to consult the MSWG (Modelling and Simulation Working Group) on the adequacy of the PK data submitted by the MAH in the context of the on-going procedure: **For adoption**	See also section 12.2 Requests for CHMP Opinion under Article 5(3)

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

No items

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)

Oxynal 10mg/5mg, 20mg/10mg
Targin 10mg/5mg, 20mg/10mg,
40mg/20mg, 5mg/2.5mg

(EMEA/A-13/1402)
(oxycodone/naloxone), Mundipharma GmbH, Mutual Recognition Procedure number: DE/H/XXXX/WS/044.

Article 13 procedure triggered by Germany on the following grounds: the benefit risk balance for the claimed indication is considered negative as the available clinical data, the proposed product information and the proposed risk minimisation measures are insufficient to assure that the risks of iatrogenic drug dependence and drug prescription abuse outweigh the benefits.

- Letter from BfArM in Germany dated 2 May 2014 notifying of an official referral under Article 13: **For information**
- Appointment of CHMP (Co)Rapporteur: **For discussion**
- List of questions: **For adoption**
- Timetable: **For adoption**

13. PHARMACOVIGILANCE ISSUES

Summary of recommendations and advice of PRAC meeting held on 5-8 May 2014: **for information**

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for May 2014: **for adoption**	
Early Notification System: May 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**	

14. INSPECTIONS

14.1. GMP Inspections

Request for GMP Inspections: **for adoption**	*Disclosure of information relating to GMP inspections will not be published as undermining the purpose of such inspections.*

14.2. GCP Inspections

Request for GCP Inspections: **for adoption**	*Disclosure of information relating to GCP inspections will not be published as undermining the purpose of such inspections.*

14.3. Pharmacovigilance Inspections

Request for Pharmacovigilance Inspections: **for adoption**	*Disclosure of information relating to Pharmacovigilance inspections will not be published as undermining the purpose of such inspections.*

14.4. GLP Inspections

Request for GLP Inspections: **for adoption**	*Disclosure of information relating to GLP inspections will not be published as undermining the purpose of such inspections.*

15. INNOVATION TASK FORCE

15.1. Minutes of ITF: For information

Minutes from the 2Q 2014 EU-Innovation Network Teleconference held on 12 May 2014: **For information**

Minutes from the March ITF Plenary held on 21 March 2014: **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.

ITF Briefing Meeting Report. Briefing Meeting held on 13 March 2014 within the margin of CAT: **For information**

ITF Briefing Meeting held on 19 May 2014 within the margin of CAT**: For information**

15.3. Eligibility to EMA scientific services

No items

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

Request from DG Sanco for EMA scientific Opinion under Article 57 (1)P of Regulation No 726/2004

- CHMP Coordinator: **To be appointed**

15.5. Nanomedicines activities

No items

16. SCIENTIFIC ADVICE WORKING PARTY (SAWP)

Report from the SAWP meeting held on 05-07 (08) May 2014. Table of conclusions: **for information**

Scientific advice letters:	*Disclosure of information relating to scientific advice letters cannot be released at present time as deemed containing commercially confidential information.*

17. SATELLITE GROUPS / OTHER COMMITTEES

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 19-21 May 2014: **for information**	
Letter from CMD(h) to QWP on dissolution specifications for Levothyroxine Vale tablets (NL/H/2700/001-011/DC): **For information** • Consultation of QWP: **For adoption**	
Letter from CMD(h) to CHMP regarding guidance on comparison of quality attributes: **For information**	

18. OTHER COMMITTEES

Committee for Orphan Medicinal Products (COMP)

Press release of the COMP meeting held on 13-14 May 2014: **for information**	To be sent in the Post-mail.

Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 5-6 May 2014: **for information**	

Paediatric Committee (PDCO)

PIPs reaching D30 at May 2014 PDCO: **for information**	To be sent in the Post-mail.
Report from the PDCO meeting held on 21-23 May 2014: **for information**	

Committee for Advanced Therapies (CAT)

Table of Decisions of CAT meeting held on 15-16 May 2014: **for information**	

19. INVENTED NAME ISSUES

Invented name issue

20. ANY OTHER BUSINESS

Procedural Advice on the CHMP, CAT & PRAC (Co-) Rapporteur appointment: **For discussion**

Composition of temporary Working Party: **For adoption**

- Biosimilar Medicinal Products Working Party
- Blood Working Party
- Infectious Diseases Working Party
- Rheumatology-Immunology Working Party
- Vaccines Working Party
- Central Nervous System Working Party Work
- Cardiovascular Working Party
- Pharmacogonomics Working Party Work
- Pharmacokinetics Working Party Work
- Oncology Working Party
- Biostatistics Working Party Work

Composition of Drafting Groups: **For adoption**

- Radiopharmaceutical Drafting Group
- Gastroenterology Drafting Group

Q&A on excipients Gluten (EMA/CHMP/704219/2013): **For adoption for 3-month public consultation**

Q&A on Benzalkonium chloride (EMA/CHMP/495737/2013): **For adoption for 3-month public consultation**

Reflection Paper on the use of Patient Reported Outcome (PRO) measures in oncology studies" following comments from the GCG: **For adoption**

- Overview of comments: **For information**

Follow-up discussion on changes regarding the processing of type II variations, introduction to rolling timetable, and changes to the AR template

- Additional two CHMP sponsors to be identified

Follow up discussion on principles for RMP revised process: **For discussion**

Mandate of new Ethics Advisory Group (EAG)

- CHMP sponsors to be appointed to revise the mandate: **For discussion**

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)*

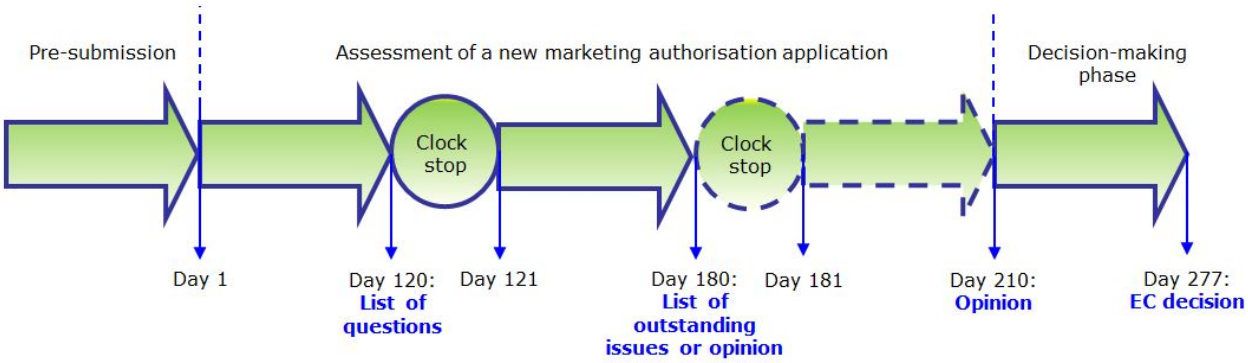
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 2 and 3) or referral procedures (section 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 a 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 a 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.