22 January 2020
EMA/CAT/41678/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 22-24 January 2020

Chair: Martina Schüßler-Lenz; Vice-Chair: Ilona Reischl

22 January 2020, 12:00 – 18:30, room 1-C

23 January 2020, 09:00 – 18:30, room 1-C

24 January 2020, 09:00 – 12:00, room 1-C

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regards to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CAT meeting reports once the procedures are finalised.

Of note, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes.

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session to be held 22-24 January 2020. See January 2020 CAT minutes (to be published post February 2020 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 22-24 January 2020 meeting

1.3. Adoption of the minutes

CAT minutes for 04-06 December 2019 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

2.7. New applications

2.7.1. Valoctocogene roxaparvovec - Orphan - EMEA/H/C/004749

Accelerated assessment

BioMarin International Limited; treatment of haemophilia A

Scope: timetable for assessment

Action: for adoption

2.8. Withdrawal of initial marketing authorisation application

No items

2.9. Re-examination of initial application procedures under Article 9(2) of Regulation No. 726/2004

No items

2.10. GMP and GCP inspections requests

No items

2.11. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0014

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: quality. Opinion

Action: for adoption

Request for Supplementary Information adopted on 08.11.2019.

2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0017/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: quality:

Request for Supplementary Information

Action: for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/ANX/002

Amgen Europe B.V.

Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen

Scope: clinical. Opinion

From initial MAA:
To submit the preliminary results from Study 20110266 (a phase 2, multicenter, randomized, open-label trial assessing the efficacy and safety of talimogene laherparepvec neoadjuvant treatment plus surgery vs surgery alone for resectable stage IIIB to IVM1a melanoma).

Action: for adoption

2.12.2. Zynteglo – autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - Orphan - EMEA/H/C/003691/R/0005

Bluebird bio (Netherlands) B.V.

Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik

Scope: 1-year renewal of conditional marketing authorisation. Request for Supplementary Information

Action: for adoption

3. Certification of ATMPs

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

3.1. Opinion

No items

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

3.4. Ongoing applications

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous, *ex vivo* expanded, clonal neoantigen specific tumour infiltrating lymphocytes

Intended for the treatment of solid tumours

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Autologous adipose derived mesenchymal stem cells, ALS

Intended for the treatment of Amyotrophic Lateral Sclerosis (ALS)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Wharton jelly derived mesenchymal stem cells

Intended for the treatment of spinal cord injury, drug resistant epilepsy and hypoxia ischemia encephalopathy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting CD19 antigen

Intended for the treatment of CD19+ haematological malignancies

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting B-cell maturation antigen (BCMA)

Intended for the treatment of relapsed or refractory multiple myeloma

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Micronized autologous adipose tissue particles and costal cartilage powder

Intended for the treatment of cartilage defects

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Human embryonic stem cell-derived otic neural progenitor cells –

Intended for the treatment of sensorineural hearing loss

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Wharton's jelly derived mesenchymal stem cells, ALS

Intended for the treatment of Amyotrophic Lateral Sclerosis (ALS)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Wharton's jelly derived mesenchymal stem cell, Huntington's disease

Intended for the treatment of Huntington's disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.10. Wharton's jelly derived mesenchymal stem cell, Lewy body dementia (LBD)

Intended for the treatment of Lewy body dementia (LBD)Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.11. Wharton's jelly derived mesenchymal stem cell, secondary progressive multiple sclerosis (SPMS)

Intended for the treatment of secondary progressive multiple sclerosis (SPMS)

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Adenovirus associated viral vector serotype 5 containing the human RPGR gene – H0005544

Intended for the treatment of X-linked retinitis pigmentosa owing to defects in the RPGR

Scope: ATMP scientific recommendation

4.2.2. Recombinant adeno-associated viral vector serotype 9 encoding a codon-optimised human aspartylglucosaminidase (AGA) transgene

Intended for the treatment of Aspartylglucosaminuria

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Adipose derived mesenchymal stem cell, Alopecia

Intended for the treatment of alopecia

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Adipose derived mesenchymal stem cell, Hypertrophic scars

Intended for the treatment of hypertrophic scars

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Wharton's jelly derived mesenchymal stem cell, AMD

Intended for the treatment of age-related macular degeneration (AMD)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Wharton's jelly derived mesenchymal stem cell , bone non-union

Intended for the treatment of bone non-union

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. Wharton's jelly derived mesenchymal stem cell, Chorioretinal disorders

Intended for the treatment of Behçet's disease, Choroideremia, Vitelliform macular dystrophy (Best disease), Cone rod dystrophies

Scope: ATMP scientific recommendation

Action: for adoption

4.2.8. Wharton's jelly derived mesenchymal stem cell, Epidermolysis bullosa -

Intended for the treatment of Epidermolysis bullosa

Scope: ATMP scientific recommendation

Action: for adoption

4.2.9. Wharton's jelly derived mesenchymal stem cell, hypoxic-ischemic encephalopathy (HIE)

Intended for the treatment of hypoxic-ischemic encephalopathy

Scope: ATMP scientific recommendation

Action: for adoption

4.3. Day 60 revised scientific recommendation (following list of questions)

No items

4.4. Finalisation of procedure

4.4.1. Autologous chondrocytes in suspension - H0005498

Intended for the treatment of knee joint cartilage lesion

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.2. Autologous chondrocytes on a fibrinogen carrier – H0005525

Intended for the treatment of knee joint cartilage lesion

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.3. Modulated immune cells – H0005515

Intended for prophylactic use in solid organ transplantation (e.g. kidney transplantation) and therapeutic use in autoimmune disease (e.g. multiple sclerosis)

Scope: minor comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.4. Wharton's jelly derived mesenchymal stem cell, Adrenoleukodystrophy – H0005526

Intended for the treatment of adrenoleukodystrophy

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.5. Wharton's jelly derived mesenchymal stem cell, Encephalopathy – H0005527

Intended for the treatment of encephalopathy

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.6. Wharton's jelly derived mesenchymal stem cell, Epilepsy – H0005528

Intended for the treatment of epilepsy

Scope: no comments raised by the European Commission. Final ATMP scientific

recommendation

Action: for information

4.4.7. Wharton's jelly derived mesenchymal stem cell, Osteoarthritis – H0005529

Intended for the treatment of osteoarthritis

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.8. Wharton's jelly derived mesenchymal stem cell, Polyneuropathy – H0005530

Intended for the treatment of polyneuropathy

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.9. Wharton's jelly derived mesenchymal stem cell, Spinal muscular atrophy – H0005531

Intended for the treatment of spinal muscular atrophy

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.10. Wharton's jelly derived mesenchymal stem cell, Spinocerebellar ataxia – H0005532

Intended for the treatment of spinocerebellar ataxia

Scope: no comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

5. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1. New requests – appointment of CAT Rapporteurs

5.2. CAT reports

5.3. List of Issues

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

6.4. Pre-submission Issues

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT Chairperson - election

Scope: election of Chairperson .

Action: for election

7.1.2. CAT membership

Romania: Alina Musetescu – new member. Membership mandate started on 17 December 2019
Romania: Simona Badoi – membership ended on 16 December 2019

Portugal: Maria-Isabel Borba Vieira – new alternate. Membership mandate started on 10 January 2020
Portugal: Margarida Menezes-Ferreira – membership ended on 31 December 2019

Action: for information

7.1.3. Seating plan for CAT members under the Croatian EU Presidency – 01 January to 30 June 2020

Scope: CAT seating plan 01 January to 30 June 2020

Action: for information

7.1.4. Revision of templates for accelerated assessment requests

CAT/CHMP: Jan Mueller-Berghaus, CHMP: Johann Lodewijk Hillege

Scope: revision of templates for accelerated assessment requests

Action: for discussion

Note: following up from discussions at CHMP in October 2019, a revised draft update to the template for the briefing note on accelerated assessment requests has been prepared, addressing comments from committee sponsors.

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Human Use (CHMP)

Scope: Summary of Outcomes (SoO) for the December 2019 meeting

Action: for information

7.2.2. CAT-COMP working group

Scope: kick-off meeting to take place. Call of interest to nominate five members from each committee (in addition to the Chair and Vice-Chairs) as participants/representatives

Action: for discussion

7.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

7.4. Cooperation within the EU regulatory network

7.4.1. Genetically modified organisms (GMO)

Scope: new procedure for the consultation of GMO authorities on the ERA for GMOs in MAAs; guidance to applicants on data to be provided in the MAA.

Action: for information

7.4.2. Concerns over the use of unregulated ATMPs

CAT: Martina Schüßler-Lenz

Scope: CAT concerns over the use of unregulated ATMPs Consideration on the need for revision on the 2010 CAT public statement.

Action: for discussion

Note: In 2010, CAT issued a public statement on concerns over unregulated medicinal products containing stem cells (https://www.ema.europa.eu/en/news/public-statement-concerns-over-unregulated-medicinal-products-containing-stem-cells). FDA and Health Canada issued similar statements in 2019 (FDA, March 2019: https://www.fda.gov/consumers/consumer-updates/fda-warns-about-stem-cell-therapies ; Health Canada, May 2019: https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/cell-therapy-policy.html). Various publications and press articles indicate that such practices are also taking place in Europe (see, e.g. Polish article *'Polityka' investigation: deceptive stem cell therapies*: https://www.polityka.pl/tygodnikpolityka/nauka/1935142,1,sledztwo-polityki-zludne-terapie-komorkami-macierzystymi.read).

7.5. Cooperation with international regulators

7.5.1. ICH S12 - guideline on biodistribution of gene therapy medicinal products

CAT: Claire Beuneu, Rune Kjeken

Scope: preparation of the ICH S12 concept paper: feedback from the drafting groups at the ICH meeting in Singapore (November 2019)

Action: for information

7.6. CAT work plan

7.6.1. CAT work plan 2020

CAT: Martina Schüßler-Lenz

Scope: draft work plan 2020

Action: for adoption

7.7. Planning and reporting

None

7.8. Others

7.8.1. EU NTC proposal for training on pharmacoepidemiology

Action: For information

8. Any other business

No items

Date of next CAT meeting:

19-21/02/2020

9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

Abbreviations / Acronyms

AAV: Adeno-Associated Virus

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Application

MAH: Marketing Authorisation Holder

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

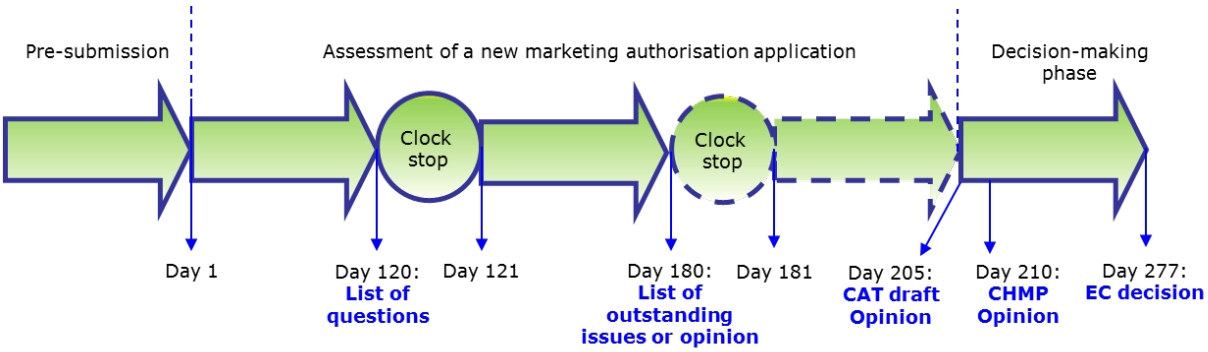
Evaluation of ATMPs (section 2)

This section lists applications for marketing authorisations of new Advanced Therapy Medicinal Products (ATMPs) that are to be discussed by the Committee. It also lists any ATMP related inspection requests (section 2.9) and Post-authorisation activities (section 2.10).

New applications (sections 2.1. to 2.12.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found here.

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 CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.3) or a List of outstanding issues to be addressed by the company, which is listed in the agenda under sections 2.7 (**Ongoing evaluation procedures**). Section 2.7 also includes the CAT discussions at any other timepoint of the evaluation procedure of new applications.

Oral explanation (section 2.2.)

Prior to adoption of the CAT opinion, marketing authorisation applicants are normally invited to the CAT plenary meeting to address questions raised by the Committee.

Oral explanations normally relate to ongoing applications, but they can also relate to any other issue for which the CAT would like to discuss with company representatives in person.

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

2.6.)

This section lists applications for new marketing authorisation for ATMPs for which the applicant has requested a re-examination of the opinion previously issued by the CHMP. Similar to the initial evaluation of a marketing authorisation of an ATMP, CAT will adopt a draft re-examination opinion, which is transmitted to the CHMP for final adoption.

Withdrawal of applications (section 2.7.)

This section includes information on marketing authorisation applications that are withdrawn by the applicant. Applicants may decide to withdraw applications at any stage during the assessment and a CAT opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

New applications (section 2.9.)

In this section, information is included on upcoming marketing authorisation applications for ATMPs, as well as information on appointment of Rapporteurs for new ATMP applications.

GMP and GCP Inspections Issues (section 2.10.)

This section lists inspections that are undertaken for ATMPs. 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).

Post-authorisation activities (section 2.12.)

This section lists type II variations, extension application according to Annex I of Reg. 1234/2008, re-examination procedures 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 and other issues concerning authorised medicines that are not covered elsewhere in the agenda such as annual reassessments, 5-year renewals, supply shortages, qualify defects. 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, will also be included here.

Certification of ATMPs (section 3)

This section includes the scientific evaluation by the CAT of quality and non-clinical data that small and medium-sized enterprises have generated at any stage of the ATMP development process. More information on the ATMP certification procedure can be found here.

Scientific Recommendation on Classification of ATMPs (Section 4)

This section includes the scientific recommendation by the CAT on whether medicines based on genes, cells or tissues meet the scientific criteria that define ATMPs. More information on the ATMP classification procedure, including the outcomes of finalised classifications, can be found here.

Scientific Advice (section 5)

This section includes all scientific advice given to companies during the development of an ATMP. Information related to the number of ATMP related scientific advices discussed by CAT can be found in the CAT Monthly reports. Further information on SAWP can be found here.

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

This section includes the discussion of an ATMP before a formal application for marketing authorisation is submitted. These cases refer for example 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.

CAT contributes to the evaluation of a Paediatric Investigation Plan (PIPs) for ATMPs by the Paediatric Committee. These PIPs are included in this section of the Agenda.

ITF Briefing meeting in the field of ATMPs

This section refers to briefing meetings of the Innovation Task Force and International co-operations activities of the CAT

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes of meetings with applicants developing ATMPs and of other ITF meetings of interest to the CAT are included in this section of the agenda. Further information on the ITF can be found here.

Priority Medicines (PRIME)

This section includes the new requests for eligibility to PRIME for ATMPs under development, the discussions in CAT of these eligibility requests and the final recommendations for eligibility of ATMPs adopted by CHMP.

CAT will appoint one of its members as the CAT sponsor for each new ATMP eligibility request who will lead the CAT discussion based on the recommendation from the SAWP.

Organisational, regulatory and methodological matters (section 7)

This section includes topics related to regulatory and procedural guidance, CAT workplan, CAT meeting organisation (including CAT membership), planning and reporting, co-ordination with other committees, working parties and scientific advisory groups.

Furthermore, this section refers to the activities of the CAT drafting groups developing scientific guidelines for gene therapy medicinal products and for cell-based medicinal products, cooperation within the EU regulatory network and international regulators as well as direct interaction with interested parties. It also includes topics of scientific interest for the Committee that are not directly related to the work of the CAT drafting groups or CAT associated working parties.

Any other business (section 8)

This section is populated with miscellaneous topics not suitable under the previous headings.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/