06 November 2019
EMA/CAT/602883/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 06-08 November 2019

06 November 2019, 14:00 – 18:30, room 0-C

07 November 2019, 09:00 – 18:30, room 0-C

08 November 2019, 09:00 – 12:00, room 0-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 regard 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 06-08 November 2019. See November 2019 CAT minutes (to be published post-December 2019 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 06-08 November 2019 meeting

1.3. Adoption of the minutes

CAT minutes for 09-11 October 2019 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Viable T-cells - Orphan - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: Opinion

Action: for adoption

List of Outstanding Issues adopted on 21.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017. Oral explanation took place on 10.10.2019.

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

2.6.1. onasemnogene abeparvovec - Orphan - EMEA/H/C/004750

AveXis Netherlands B.V.; treatment of spinal muscular atrophy (SMA)

Sope: feedback from Rapporteurs

Action: for discussion

2.6.2. onasemnogene abeparvovec - Orphan - EMEA/H/C/004750

AveXis Netherlands B.V.; treatment of spinal muscular atrophy (SMA)

Scope: SmPC

Action: for discussion

2.7. New applications

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

Ni items

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

2.11.1. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/II/0009

Takeda Pharma A/S

Rapporteur: Lisbeth Barkholt

Scope: quality. Request for supplementary information (RSI).

Action: for adoption

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

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: quality. Request for supplementary information (RSI).

Action: for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - Orphan - EMEA/H/C/002450/R/0026

Chiesi Farmaceutici S.p.A.

Rapporteur: Egbert Flory; CHMP Coordinator: Jan Mueller-Berghaus; PRAC Rapporteur: Julie

Williams

Scope: 5th annual reassessment for the renewal of marketing authorisation. Opinion

Action: for adoption

2.12.2. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854/ANX/004.2

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruiz, CHMP Coordinator: Greg Markey

Scope: PASS interim study report /ADA-SCID) Registry
Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID) Registry for Patients Treated with Strimvelis™ (or GSK2696273) Gene Therapy: Long-Term Prospective, Non-Interventional Follow-up of Safety and Effectiveness. PRAC advice to CAT.

Action: for adoption

2.12.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/009.1

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Pharmacovigilance: Submission of the protocol for study CCTL019H2301, a randomized open-label parallel-group multicenter Phase III trial to evaluate the efficacy and safety of tisagenlecleucel in adult patients with relapsed or refractory B-cell aggressive NHL after failure of rituximab and anthracycline containing first-line immunochemotherapy. Study data will support further characterization of the benefit-risk ratio of tisagenlecleucel in an earlier line of DLBCL. PRAC assessment report.

Action: for adoption

2.12.4. Yescarta – axicabtagene ciloleucel – Orphan – EMEA/H/C/4480 - EMEA/G/C/PSUSA/00010703/201904

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus; PRAC Rapporteur: Anette Kirstine-Stark

Scope: Pharmacovigialnce: evaluation of a PSUSA procedure. PRAC recommendation

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

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous chondrocytes in suspension - H0005498

Intended for the treatment of knee joint cartilage lesion

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

Autologous chondrocytes on a fibrinogen carrier Intended for the treatment of knee joint cartilage lesion

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. MICs - Modulated immune cells

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Wharton's Jelly derived mesenchymal stem cell , Adrenoleukodystrophy

Intended for the treatment of adrenoleukodystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Wharton's Jelly derived mesenchymal stem cell , Encephalopathy

Intended for the treatment of encephalopathy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Wharton's Jelly derived mesenchymal stem cell , Epilepsy

Intended for the treatment of epilepsy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Wharton's Jelly derived mesenchymal stem cell , Osteoarthritis

Intended for the treatment of osteoarthritis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Wharton's Jelly derived mesenchymal stem cell , Polyneuropathy

Intended for the treatment of polyneuropathy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Wharton's Jelly derived mesenchymal stem cell , Spinal muscular atrophy

Intended for the treatment of spinal muscular atrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Wharton's Jelly derived mesenchymal stem cell , Spinocerebellar ataxia

Intended for the treatment of spinocerebellar ataxia

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Recombinant adeno associated viral vector serotype 9 containing the human CLN6 gene Amicus – H0005491

Intended for the treatment of neuronal ceroid lipofuscinosis type 6 (CLN6) disease (CLN6 Batten disease)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Recombinant adeno associated viral vector serotype 9 containing the human CLN3 gene – H0005492

Intended for the treatment of neuronal ceroid lipofuscinosis type 3 (CLN3) disease (CLN3 Batten disease)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Wharton's Jelly derived mesenchymal stem cell , Alopecia areata – H0005494

Intended for the treatment of alopecia areata

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Wharton's Jelly derived mesenchymal stem cell , Pervasive developmental disorder – H0005502

Intended for the treatment of pervasive developmental disorder

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Wharton's Jelly derived mesenchymal stem cell , Cerebral infarction – H0005503

Intended for the treatment of cerebral infarction

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Wharton's Jelly derived mesenchymal stem cell , Development delay – H0005504

Intended for the treatment of development delay

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. Wharton's Jelly derived mesenchymal stem cell , Diabetes - H0005505

Intended for the treatment of diabetes

Scope: ATMP scientific recommendation

Action: for adoption

4.2.8. Wharton's Jelly derived mesenchymal stem cell , Muscular dystrophy – H0005506

Intended for the treatment of muscular dystrophy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.9. Wharton's Jelly derived mesenchymal stem cell , Endometrial atrophy – H0005507

Intended for the treatment of endometrial atrophy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.10. Wharton's Jelly derived mesenchymal stem cell , Multiple sclerosis – H0005508

Intended for the treatment of multiple sclerosis

Scope: ATMP scientific recommendation

Action: for adoption

4.2.11. Wharton's Jelly derived mesenchymal stem cell , Optic neuropathy – H0005509

Intended for the treatment of optic neuropathy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.12. Wharton's Jelly derived mesenchymal stem cell , Premature ovarian failure – H0005510

Intended for the treatment of premature ovarian failure

Scope: ATMP scientific recommendation

Action: for adoption

4.2.13. Wharton's Jelly derived mesenchymal stem cell , Retinitis pigmentosa – H0005511

Intended for the treatment of retinitis pigmentosa

Scope: ATMP scientific recommendation

Action: for adoption

4.2.14. Wharton's Jelly derived mesenchymal stem cell , Spina bifida – H0005512

Intended for the treatment of spinal bifida

Scope: ATMP scientific recommendation

Action: for adoption

4.2.15. Wharton's Jelly derived mesenchymal stem cell , Spinal cord injury – H0005513

Intended for the treatment of spinal cord injury

Scope: ATMP scientific recommendation

Action: for adoption

4.2.16. Wharton's Jelly derived mesenchymal stem cell , Stargardt disease – H0005514

Intended for the treatment of Stargardt disease

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. Recombinant adeno-associated virus (AAV) vector based on the AAV serotype hu37 (AAVhu37) expressing human Factor VIII - H0005490

Intended for the treatment of haemophilia A

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

Action: for information

4.5. Follow-up and guidance

No items

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

No items

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

6.3.4. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. Strategic Review & Learning meeting – Helsinki, Finland, 21 – 22 November 2019

CAT: Martina Schüßler-Lenz, Heli Suila

Scope: draft agenda of the joint meeting PDCO-COMP-CAT

Action: for discussion

7.1.2. Strategic Review & Learning meeting – joint CAT/Clinical trial facilitation group (CTFG), Bucharest, Romania, June 2019

CAT: Simona Badoi

Scope: minutes from the SRLM meeting

Action: for information

A short oral feedback was provided in July 2019.

7.1.3. Survey on CAT members' accessibility of EMA's technical tools

Scope: outcome of the survey on the accessibility of the technical tools available to CAT members

Action: for information

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 October 2019 meeting

Action: for information

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

7.3.1. Questions & Answers on comparability

CAT drafting group: Margarida Menezes, Ilona Reischl, Ivana Haunerová, Heli Suila, Barbara Bonamassa

Scope: draft questions and answers document

Action: for information

Note: the document is for adoption by CAT at its December 2019 meeting.

7.4. Cooperation within the EU regulatory network

No items

7.5. Cooperation with international regulators

7.5.1. ATMP cluster teleconference with FDA-USA, Health Canada and PMDA-Japan

The teleconference will take place on Thursday 14 November, 15:00 – 16:00hrs

Scope: draft agenda

Action: for discussion

7.5.2. International Pharmaceutical Regulators Programme (IPRP) – Gene therapy working group

CAT: Pille Säälik

Scope: feedback on the teleconference that took place on 23 October 2019

Action: for information

7.6. CAT work plan

7.6.1. CAT work plan 2020

CAT: Martina Schüßler-Lenz

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. CAT regulatory session at the 2019 Annual Congress of the European Society of Gene and Cell Therapy (ESGCT), 25 October 2019, Barcelona (Spain)

CAT: Martina Schüssler-Lenz, Jan Müller-Berghaus, Anne Pastoft, Heli Suila

Scope: feedback on the CAT session at the ESGCT annual congress

Action: for information

7.8.2. Curriculum on Advanced Therapies Medicinal Products (ATMPs) - training session on quality aspects for cell-based medicinal products

CAT: Margarida Menezes Ferreira

Scope: training session on quality aspects for cell-based medicinal products to take place on 6th December 2019, 13:00hrs-13:50hrs (tbc)

Action: for information

8. Any other business

8.1.1. EMA relocation to the permanent building, Amsterdam, The Netherlands

Scope: update on planned timelines

Action: for information

8.1.2. Heads of Medicines Agencies (HMA)-EMA joint big data taskforce - draft recommendations

Scope: HMA-EMA Joint Big Data Taskforce summary report

Action: for discussion

8.1.3. Future-proofing EMA

Action: for information

Date of next CAT meeting:
04-06 December 2019

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

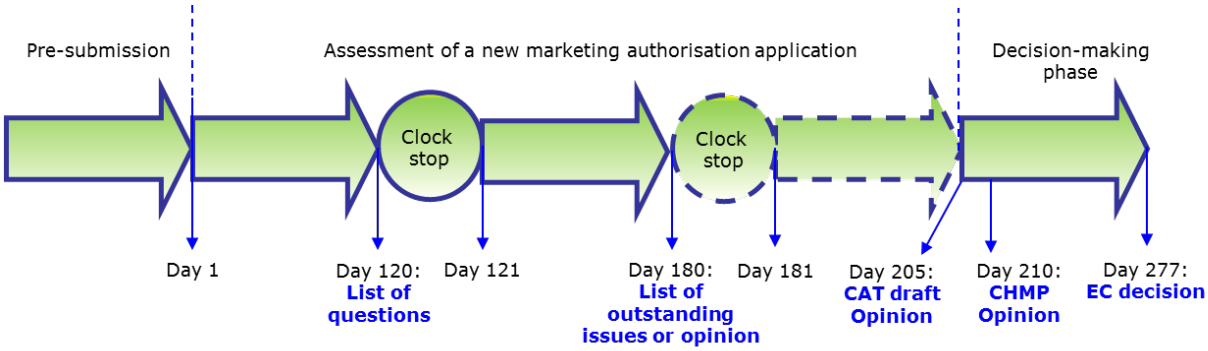
Evaluation of ATMPs (section 2)

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/