09 October 2019
EMA/CAT/556528/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 09-11 October 2019

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

09 October 2019, 14:00 – 18:30, room 0-C

10 October 2019, 09:00 – 18:30, room 0-C

11 October 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 09-11 October 2019. See October 2019 CAT minutes (to be published post-November 2019 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 09-11 October 2019 meeting

1.3. Adoption of the minutes

CAT minutes for 11-13 September 2019 meeting

1.4. Technical information

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

2.2.1. 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: oral explanation

Action: for discussion

List of Outstanding Issues adopted on 21.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

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

No items

2.7. New applications

2.8. Withdrawal of initial marking 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. 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/II/0022

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruiz

Scope: safety: submission of an updated RMP version 2.0 in order to introduce changes to the design of the post-authorisation study STRIM-002, from a prospective to a retrospective study. Following additional minor changes to the RMP are also included: Update of the RMP in line with EMA Rev.2.0.1 template; update of the RMP to make the necessary amendments to the name of the MAH following the MAH transfer; update of the data in the RMP in line with the updated data lock point; update of timelines for the STRIM-001 study. Opinion

Action: for adoption

2.11.2. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0011

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality Opinion

Action: for adoption

Request for Supplementary Information adopted on 13.09.2019.

See also 2.12.2 and 2.12.3.

2.11.3. Zalmoxis - nalotimagene carmaleucel - Orphan - EMEA/H/C/002801/II/0016

MolMed S.p.A

Rapporteur: Carla Herberts; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Proposal from the MAH to terminate the study TK008 (specific obligation for the CMA) and replace it with study TK013. .

Action: for information

Request for Supplementary Information adopted on 19.07.2019

2.11.4. Zalmoxis - nalotimagene carmaleucel - Orphan - EMEA/H/C/002801/R/0015

MolMed S.p.A

Rapporteur: Carla Herberts; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: update on the status of the annual renewal.

Action: for discussion

2.11.5. Zynteglo - Orphan - EMEA/H/C/003691/II/0001-G

Bluebird bio (Netherlands)

Rapporteur: Carla Herberts

Scope: quality: opinion

Action: for adoption

2.12. Other Post-Authorisation Activities

2.12.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090

Novartis Europharm Limited

Rapporteur: Rune Kjeken; CHMP coordinator: Bjorg Bolstad; PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: CAR-T cell imposed PASS studies: issues with implementation and current status; feedback from PRAC discussion.

Action: for discussion

2.12.2. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/MEA/003.1

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated protocol for study KT-EU-471-0116 assessing Health Care Provider's awareness and knowledge of the routine and additional Risk Minimisation Measures addressing the key important identified risks associated with the use of Yescarta and their understanding of the handling and administration of Yescarta. Responses to PRAC RSI of 14 June 2019 are included.

Action: for adoption

See also 2.11.2. and 2.12.3.

2.12.3. YESCARTA - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark

Scope: CAR-T cell imposed PASS studies: issues with implementation and current status; feedback from PRAC discussion.

Action: for discussion

See also 2.11.2 and 2.12.2.

2.12.4. 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. RSI

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

3.3. New Applications

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Recombinant adeno associated viral vector serotype 9 containing the human CLN6 gene Amicus

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Recombinant adeno associated viral vector serotype 9 containing the human CLN3 gene

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

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Wharton's Jelly derived mesenchymal stem cell , Alopecia areata

Intended for the treatment of alopecia areata

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Wharton's Jelly derived mesenchymal stem cell , Pervasive developmental disorder

Intended for the treatment of pervasive developmental disorder

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Wharton's Jelly derived mesenchymal stem cell , Cerebral infarction

Intended for the treatment of cerebral infarction

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Wharton's Jelly derived mesenchymal stem cell , Development delay

Intended for the treatment of development delay

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

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

Intended for the treatment of diabetes

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Wharton's Jelly derived mesenchymal stem cell , Muscular dystrophy

Intended for the treatment of muscular dystrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Wharton's Jelly derived mesenchymal stem cell , Endometrial atrophy

Intended for the treatment of endometrial atrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.10. Wharton's Jelly derived mesenchymal stem cell , Multiple sclerosis

Intended for the treatment of multiple sclerosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.11. Wharton's Jelly derived mesenchymal stem cell , Optic neuropathy

Intended for the treatment of optic neuropathy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.12. Wharton's Jelly derived mesenchymal stem cell , Premature ovarian failure

Intended for the treatment of premature ovarian failure

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.13. Wharton's Jelly derived mesenchymal stem cell , Retinitis pigmentosa

Intended for the treatment of retinitis pigmentosa

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.14. Wharton's Jelly derived mesenchymal stem cell , Spina bifida

Intended for the treatment of spinal bifida

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.15. Wharton's Jelly derived mesenchymal stem cell , Spinal cord injury

Intended for the treatment of spinal cord injury

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.16. Wharton's Jelly derived mesenchymal stem cell , Stargardt disease

Intended for the treatment of Stargardt disease

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 virus (AAV) vector based on the AAV serotype hu37 (AAVhu37) expressing human Factor VIII

Intended for the treatment of haemophilia A

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. Adipose-derived mesenchymal stem cells - H0005458

Intended for the treatment of diabetic foot ulcers (DFU)

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

Action: for information

4.4.2. Human allogeneic melanoma cells Mich1H6 and Mich2H6 - H0005459

Intended for the treatment of advanced melanoma (stage IIIB-IV)Scope: comments raised by the European Commission. Final ATMP scientific recommendation

Action: for information

4.4.3. CD1c(BDCA-1)+/CD141(BDCA-3)+ myeloid dendritic cells - H0005460

Intended for the treatment of patients with advanced, pre-treated solid tumours with injectable metastases

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

Action: for information

4.4.4. Human autologous Adipose Tissue - derived Mesenchymal Stem / Stromal Cells (AT-MSCs) – H0005461

Intended for the treatment of bone and cartilage defects including osteoarthritis

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

Action: for information

4.4.5. Oncolytic adenovirus – H0005463

Intended for the treatment-naïve patients with localized prostate cancer

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

Action: for information

4.4.6. Platelet-Rich Stroma (PRS) - combination of platelet-rich plasma and stromal vascular fraction – H0005430

Intended for wound healing as additional therapy to fistula surgery in patients with complex and therapy refractory perianal fistula

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

Action: for information

4.4.7. *In vitro* transcribed mRNA encoding the human insulin-like growth factor 1 (IGF-1) – H0005462

Intended for the treatment of skeletal muscle injury

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

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: Heli Suila

Scope: draft agenda for the CAT-only session

Action: for discussion

Note: CAT at its September already made proposals for the agenda of the joint CAT-PDCO-COMP session and the joint CAT-COMP session. Awaiting feedback from COMP and PDCO.

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 September 2019 meeting

Action: for information

7.2.2. Scientific Coordination Board (SciCoBo) – meeting of 25 September 2019

CAT: Martina Schüßler-Lenz

Scope: feedback on the outcome of the SciCoBo meeting that took place on 25 September 2019

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 discussion

7.4. Cooperation within the EU regulatory network

7.4.1. Interplay with GMO framework: new initiatives

Scope: feedback from a meeting between the GMO and medicines authorities on environmental risk assessment of GTMPs in clinical trials

Action: for information

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

CAT: Martina Schüßler-Lenz

Scope: preparation of the next ATMP cluster

Action: for discussion

7.5.2. Blood cluster teleconference with US-FDA and Health Canada

Scope: agenda of the blood cluster TC

Action: for information

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

CAT: Pille Säälik

Scope: agenda of the IPRP-gene therapy working group

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

None

7.8. Others

7.8.1. Curriculum on Advanced Therapies Medicinal Products (ATMPs) training

CAT: Ilona Reischl

Scope: plan of trainings for the end of 2019 and beginning of 2020

Action: for discussion

7.8.2. Harmonisation of communication subject naming convention received from NCAs

Action: for information

8. Any other business

No items

Date of next CAT meeting:

06-08 November 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

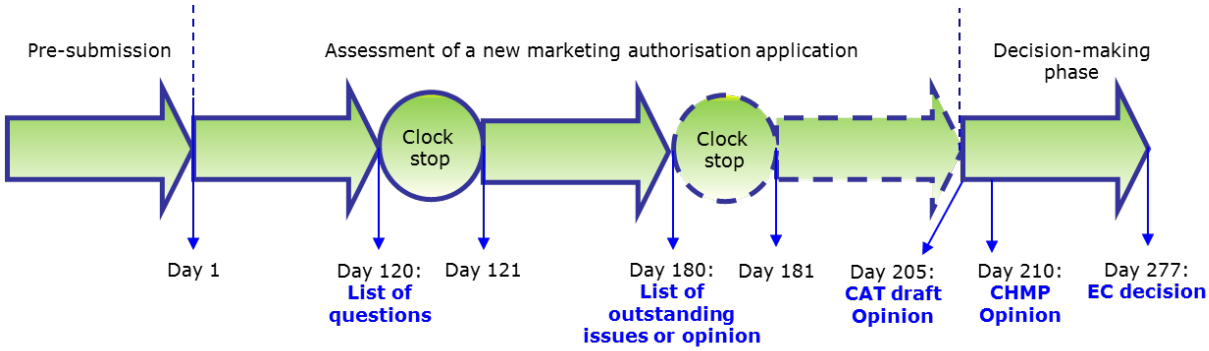
Evaluation of ATMPs (section 2)

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/