22 April 2020
EMA/CAT/220061/2020
Human Medicines Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 22-24 April 2020

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

22 April 2020, 14:00 – 18:30, virtual meeting

23 April 2020, 09:00 – 18:30, virtual meeting

24 April 2020, 09:00 – 12:00, virtual 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 22-24 April 2020. See April 2020 CAT minutes (to be published post-May 2020 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 22-24 April 2020 meeting

1.3. Adoption of the minutes

CAT minutes for 18-20 March 2020 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

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

Accelerated assessment

BioMarin International Limited; treatment of haemophilia A

Scope: Day 120 list of questions

Action: for adoption

2.5. Day 80 assessment reports

2.5.1. Autologous anti-CD19-transduced CD3+ cells - Orphan - EMEA/H/C/005102

Accelerated assessment

Kite Pharma EU B.V.; treatment of adult patients with relapsed or refractory Mantle cell lymphoma (MCL)

Scope: Day 80 assessment report

Action: for information

2.5.2. Eladocagene exuparvovec - Orphan - EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino aciddecarboxylase (AADC) deficiency

Scope: Day 80 assessment report

Action: for information

2.6. Update on ongoing initial applications

No items

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

No items

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

2.11.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0036

Amgen Europe B.V.

Rapporteur: Olli Tenhunen

Scope: quality: Opinion

Action: for adoption

Request for Supplementary Information adopted on 21.02.2020.

2.11.2. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0015

CO.DON AG

Rapporteur: Lisbeth Barkholt, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: safety: Request for supplementary information
update of section 4.8 and 5.1 of the SmPC following the 48-month follow up data for trial cod 16 HS 13, a study assessing the long-term efficacy and safety of Spherox.

Action: for adoption

2.11.3. 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/0024

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruiz, PRAC Rapporteur: Menno van der Elst

Scope: safety: Opinion
Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information following the completion of the STRIM-004 study, which is a non-interventional long term follow up of the subjects who received Strimvelis gene therapy. This study included paediatric patients and is listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor administrative changes in the PI.

Action: for adoption

Request for Supplementary Information adopted on 20.03.2020.

2.11.4. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0015

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality: Request for supplementary information (RSI)

Action: for adoption

Request for Supplementary Information adopted on 21.02.2020.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/REC/007

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: quality

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

3.2. Day 60 Evaluation Reports

No items

3.3. New Applications

No items

4. Scientific Recommendation on Classification of ATMPs

4.1.1. Recombinant adeno-associated viral vector (serotype 8) carrying an optimised gene for human cyclic nucleotide gated channel subunit beta 3 (CNGB3) protein

Intended for the treatment of achromatopsia caused by mutations in the CNGB3 gene

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Genetically modified Lactococcus lactis strain sAGX0407, engineered to secrete human pro-insulin and human IL-10

Intended for the treatment of clinical recent-onset Type 1 diabetes mellitus

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Autologous CD34+ cells transduced with a lentiviral vector encoding a modified γ-globin gene

Intended for the treatment of sickle cell disease (SCD) and β -thalassemia

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Human autologous hematopoietic stem cells transduced with a lentiviral vector containing codon-optimized cDNA encoding for functional human alpha galactosidase

Intended for the treatment of Fabry disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Human autologous hematopoietic stem cells transduced with a lentiviral vector containing codon-optimized cDNA encoding for functional human glucocerebrosidase

Intended for the treatment of Gaucher disease

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Wharton's jelly derived mesenchymal cells– H000

Intended for the treatment of patients with Covid-19 infections

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. Wharton's jelly derived mesenchymal stem cell , Covid-19

Intended for the treatment of patients with Covid-19 infections

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. Wharton's jelly derived mesenchymal stem cell , Optic atrophy

Intended for the treatment of optic atrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.9. Wharton's jelly derived mesenchymal stem cell , IFAP syndrome

Intended for the treatment of patients with IFAP syndrome

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.10. Wharton's jelly derived mesenchymal stem cell , Bone marrow transplant rejection

Intended for the treatment of bone marrow transplant rejection

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.11. Wharton's jelly derived mesenchymal stem cell , Secondary graft failure

Intended for the treatment of secondary bone marrow transplant failure/ secondary graft failure

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.12. Wharton's jelly derived mesenchymal stem cell , Progressive Supranuclear Palsy

Intended for the treatment of progressive Supranuclear Palsy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.13. Wharton's jelly derived mesenchymal stem cell , Multiple system atrophy

Intended for the treatment of multiple system atrophy

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Gene-activated matrix based on octacalcium phosphate and a plasmid carrying VEGF-A gene – H0005629

Intended to various bone healing indications (sinus lift, non-unions, spinal fusion, etc.)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Leuco platelet enriched plasma – H0005630

Intended for the treatment of ulcers, chronic wounds

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Recombinant adeno-associated viral vector rh74 containing the human beta-sarcoglycan gene – H0005631

Intended for the treatment of limb-girdle muscular dystrophy type 2E

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Wharton's jelly derived mesenchymal stem cell, drug resistant epilepsy

Intended for the treatment of drug resistant epilepsy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Autologous adipose-derived mesenchymal stem cell, diabetic foot syndrome

Intended for the treatment of diabetic foot syndrome

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Wharton's jelly derived mesenchymal stem cell, Behcet disease

Intended for the treatment of Behcet disease

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. Wharton's jelly derived mesenchymal stem cell, choroideremia

Intended for the treatment of choroideremia

Scope: ATMP scientific recommendation

Action: for adoption

4.2.8. Wharton's jelly derived mesenchymal stem cell, foetal alcohol syndrome

Intended for the treatment of foetal alcohol syndrome

Scope: ATMP scientific recommendation

Action: for adoption

4.2.9. Wharton's jelly derived mesenchymal stem cell, frontotemporal dementia

Intended for the treatment of frontotemporal dementia

Scope: ATMP scientific recommendation

Action: for adoption

4.2.10. Wharton's jelly derived mesenchymal stem cell, progressive bulbar palsy

Intended for the treatment of progressive bulbar palsy

Scope: ATMP scientific recommendation

Action: for adoption

4.2.11. Wharton's jelly derived mesenchymal stem cell, vitelliform macular degeneration

Intended for the treatment of vitelliform macular degeneration (Best disease)

Scope: ATMP scientific recommendation

Action: for adoption

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

4.3.1. Recombinant chimeric vesicular stomatitis virus carrying the envelope glycoprotein (GP) of the visceral non-neurotropic strain of the lymphocytic choriomeningitis virus – H0005624

Intended for the treatment of solid tumours, including non-small cell lung carcinoma.

Scope: Responses from the applicant to the LoQs. Revised ATMP scientific recommendation

Action: for adoption

Request for List of Questions adopted on 20.03.2020.

4.4. Finalisation of procedure

4.4.1. Autologous CD34+ cells transduced with CL20-4i-EF1α-hγc-OPT lentiviral vector – H0005602

Intended for the treatment of X-linked severe combined immunodeficiency (XSCID)

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

Action: for information

4.4.2. Wharton's jelly derived mesenchymal stem cells, AMN – H0005623

Intended for the treatment of adrenomyeloneuropathy (AMN)

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

Action: for information

4.5. Follow-up and guidance

4.5.1. Autologous adipose-derived mesenchymal stem cells *ex-vivo* expanded, osteoarthritis – H0005529

Intended for the treatment of osteoarthritis

Scope: corrigendum to the classification report adopted at the November 2019 CAT meeting

Action: for adoption

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

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

6.3.4. Ongoing support

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Austria: Silke Dorner– Membership alternate mandate started on 31 March 2020

Action: for information

7.1.2. Strategic Review & Learning meeting (SRLM) – Budapest, Hungary, 08 – 10 June 2020

CAT: Katalin Lengyel

Scope: topics for inclusion in the joint CAT-PDCO agenda and CAT-only agenda to take place on 08-10 June 2020

Action: for discussion

7.1.3. Strategic Review & Learning meeting (SRLM) – Helsinki, Finland, 21 – 22 November 2019

CAT: Heli Suila

Scope: minutes of the meeting that took place on 21-22 November 2019

Action: for adoption

N.B. CAT members (and especially the speakers) were asked to provided comment on the minutes of the SRLM meeting to CAT secretariat by 10 April 2020.

7.1.4. CAT's Rules of Procedures

Scope: revised CAT Rules of Procedure

Action: for information

19.03.20: EMA Management Board (MB) adopted the amendments to the existing Rules of Procedure
20.03.20: CAT adopted the amendments to the existing Rules of Procedure

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 March 2020 meeting

Action: for information

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

7.3.1. Quality Review of Documents (QRD)

Scope: information on the expression of the strength and the type of cells in SmPC (sections 1 and 2)

Action: for information

Note: during the March CAT meeting, feedback was provided from the discussion in the QRD on the use of scientific notification in the expression of strength and information on the type of cells (SmPC sections 1 and 2).

7.3.2. Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells

CAT Rapporteur: Marcos Timón / Martina Schüssler-Lenz

Scope: comments received on the clinical section of the guideline: design of the confirmatory trials for CAR-T cell products

Action: for discussion

Note: during the finalisation of the guideline for external consultation, the requirement for randomized controlled trials (RCTs) for CAR-Ts was strengthened. External commenters indicate that the guideline text does not match current experience. CAT is asked to reflect on 'Single arm trials *vs.* RCTs'.

7.4. Cooperation within the EU regulatory network

7.4.1. Public statement on the use of unregulated/unproven ATMPs

Scope: EMA/CAT public statement on the use of unproven cell therapies

Action: for adoption

Note: the public statement developed by CAT in February 2020 was reworded, with the help of the EMA Communication and Press Office colleagues, the CAT chair and the CAT draft group, to make it easier to understand for the patients. The public statement is brought to the plenary meeting for adoption.

7.5. Cooperation with international regulators

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

Scope: draft agenda for the teleconference that will take place on 30 April 2020 15:00hrs

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 26 March 2020

Action: for information

7.6. CAT work plan

None

7.7. Planning and reporting

None

7.8. Others

None

8. Any other business

8.1. Participation of CAT members/alternates as speakers or panellist to international conferences

Scope: criteria for participation to international conferences

Action: for discussion

Date of next CAT meeting:

18-20/05/2020

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

EU NTC: European Union Network Training Centre

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

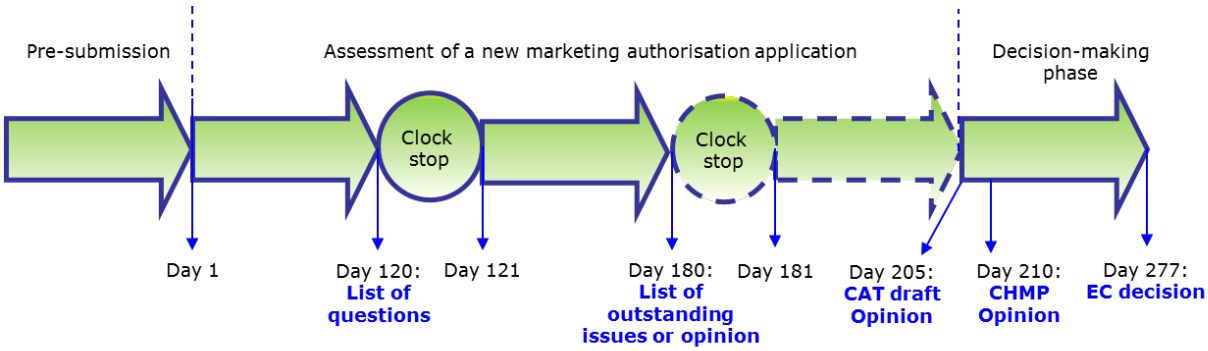
Evaluation of ATMPs (section 2)

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/