05 October 2022
EMA/CAT/772339/2022
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 05-07 October 2022

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

05 October 2022, 14:00 – 18:30, room 01-D

06 October 2022, 09:00 – 18:30, room 01-D

07 October 2022, 09:00 – 13:00, room 01-D

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 05-07 October 2022. See 05-07 October 2022 CAT minutes (to be published post 03-04 November 2022 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 05-07 October 2022 meeting

1.3. Adoption of the minutes

CAT minutes for 07-09 September 2022 meeting

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. Tabelecleucel - PRIME - Orphan - EMEA/H/C/004577

Atara Biotherapeutics Ireland Limited; treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV$^+$ PTLD)

Scope: Opinion

Action: for adoption

List of Questions adopted on 18.03.2022; List of outstanding issue adopted on 09.09.2022.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

2.3.1. Etranacogene dezaparvovec - PRIME - Orphan - EMEA/H/C/004827

CSL Behring GmbH; treatment of adults with Haemophilia B

Scope: Day 180 list of outstanding issues

Action: for adoption

List of Questions adopted on 15.07.2022.

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 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 and variations of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0003

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality. Request for Supplementary Information

Action: for adoption

Request for Supplementary Information adopted on 15.07.2022.

2.11.2. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0057

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Safety. Opinion

Update to sections 4.4 and 4.8 of the SmPC to revise the safety instructions regarding the risk of disseminated herpetic infection adverse drug reactions following an MAH review of aggregate safety data of herpetic and disseminated herpetic infections that were reported in patients who were not immunocompromised and those who were immunocompromised. The Package Leaflet is updated accordingly.

Action: for adoption

2.11.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0053

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical. Opinion

Submission of the final report from study CCTL019H2301 (BELINDA) listed as an obligation in the Annex II of the Product Information. This is a randomized open-label parallel-group multicentre 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 immune-chemotherapy. The Annex II is updated accordingly.

Action: for adoption

Request for Supplementary Information adopted on 13.05.2022.

2.11.4. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0059

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Safety and efficacy. Opinion

Update of section 5.1 of the SmPC based on a subgroup analysis from CCTL019B2401 (B2401) disease registry listed as a PAES (ANX006) in the Annex II; this is a non-interventional study to evaluate the efficacy and safety of Kymriah in ALL patients below the age of 3 years. In addition, the MAH took the opportunity to update Annex II.D of the SmPC to reflect the fulfilment of the PAES.

Action: for adoption

Request for Supplementary Information adopted on 15.07.2022.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/002

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

Scope: Quality

Action: for adoption

2.13.2. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/003

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality

Action: for adoption

2.13.3. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/011

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality

Action: for adoption

2.13.4. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/REC/012

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality

Action: for adoption

2.13.5. Luxturna - voretigene neparvovec - Orphan - EMEA/H/C/004451/REC/009

Novartis Europharm Limited

Rapporteur: Sol Ruiz

Scope: Quality

Action: for adoption

2.13.6. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/SOB/002

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Study PTC-AADC-MA-406: a real-world, multicentre, observational and longitudinal study of patients with aromatic L amino acid decarboxylase (AADC) deficiency and with a severe phenotype treated with Upstaza globally, based on data from a registry, according to an agreed protocol. From initial MAA.

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

4. Scientific Recommendation on Classification of ATMPs

Timetable:

-Start of the procedure:	07.10.2022
-EMA Coordinator's draft report:	21.10.2022
-CAT Coordinator's comments:	26.10.2022
-Revised scientific recommendation:	28.10.2022
-CAT's discussion of scientific recommendation:	04.11.2022

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic adipose-derived mesenchymal stem cells (ADMSCs)

Intended for the treatment of osteoarthritis of the knee and hip

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Allogeneic adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

Scope: ATMP scientific recommendation

Action: for adoption

4.2.2. Autologous adipose derived mesenchymal stem cells

Intended for the treatment of Crohn-related perianal fistula

Scope: ATMP scientific recommendation

Action: for adoption

4.2.3. Autologous anti-BCMA CAR-T cells

Intended for the treatment of multiple myeloma

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Allogeneic latency-2 Epstein-Barr virus-targeted cytotoxic T lymphocytes

Intended for the treatment of multiple sclerosis

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. E1-deleted (replication defective) recombinant human adenovirus serotype 5 expressing TIMP3 (tissue inhibitor of metalloproteinases-3) under the control of the cytomegalovirus immediate early promoter

Intended for the treatment of coronary artery disease requiring artery bypass grafting (CABG)

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. Autologous CD34+ cells transfected with a lentiviral vector containing codon-optimised RPS19 gene

Intended for the treatment of transfusion-dependent, steroid-resistant paediatric patients with Diamond-Blackfan anaemia, who have a mutation in the RPS19 gene

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 cultured limbal epithelial and limbal epithelial stem cells growing on fibrin scaffold

Intended for the treatment of moderate to severe limbal stem cell deficiency (LSCD) caused by burns, including chemical burns to the eyes

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

Action: for adoption

4.4.2. Human allogeneic cardiac progenitor cell subpopulation selected for the absence of the surface marker CD90

Intended to improve cardiac perfusion and function in patients with refractory angina

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

Action: for adoption

4.4.3. Allogeneic CD33-directed genetically modified T-cell immunotherapy

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

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

Action: for adoption

4.4.4. Allogeneic CRISPR/Cas9-edited hematopoietic stem and progenitor cells (HSPCs) lacking CD33 protein expression

Intended for the treatment of patients with CD33-positive acute myeloid leukaemia (AML) who are at a high risk of relapse

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

Action: for adoption

4.5. Follow-up and guidance

4.5.1. Ex-vivo expanded allogeneic human corneal epithelial cells containing P63 positively expressing cells

Intended for the treatment of persistent corneal epithelial defects

Scope: Updated ATMP scientific recommendation

Action: for adoption

Note: The report has been updated following a request for clarification received from the applicant.

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

5.1.1. Ongoing scientific advice procedures - Appointment of CAT Peer Reviewers

Timetable:

- Start of procedure at SAWP:	26-29.09.2022
- Appointment of CAT Peer Reviewers:	05-07.10.2022
- SAWP first reports:	17.10.2022
- CAT Peer Reviewer comments (NC,C):	21.10.2022
- CAT Peer reviewer comments (Q):	26.10.2022
- Discussion at SAWP:	24-27.10.2022
- Discussion at CAT and feedback to SAWP:	04.11.2022

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	24-27.10.2022
- Appointment of CAT Peer Reviewers:	03-04.10.2022
- SAWP first reports:	21.11.2022
- CAT Peer Reviewer comments:	25.11.2022
- Discussion at SAWP:	30.11.2022
- Discussion at CAT and feedback to SAWP:	01.12.2022

5.2. Procedures discussed at SAWP – 1st reports, D40 JRs, LoIs

5.3. Finalisation of D70 procedures – feedback from the discussion meeting

5.4. Final Advice Letters for procedures finalised the previous month

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

Timetable for assessment:

Procedure start:	26-29.09.2022
SAWP recommendation:	27.10.2022
CAT recommendation:	04.11.2022
CHMP adoption of report and final recommendation:	10.11.2022

No items

6.3.2. Month 1 – Discussion of eligibility

No items

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. CAT membership

No items

7.1.2. Vote by proxy

No items

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Czechia presidency, 17 – 18 November 2022 in Paris

CAT: Petr Soukup, Martina Schuessler-Lenz

Scope: updated agenda content

Action: for discussion

7.1.4. Update on procedure for Chair election

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. Guideline on Safety and Efficacy Follow-up and RMP

CAT: Martina Schüssler-Lenz / Ilona Reischl

Scope: Finalisation of the guideline

Action: for discussion

7.2.2. Scientific coordination board

CAT: Martina Schüssler-Lenz

Scope: oral feedback

Action: for information

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

7.3.1. Reflection paper on criteria to be considered for the evaluation of new active substance (NAS) status of biological substances

Rapporteur: Martijn van der Plas

Action: For adoption

7.4. Cooperation with the EU regulatory network

7.4.1. Regulatory & scientific conference on RNA-based medicines

Scope: Draft agenda of the conference that is scheduled to take place on 2 February 2023.

Action: for discussion

7.4.2. Revision of the EU legislation on blood, tissues and cells (BTC)

CAT: Ilona Reischl

Scope: Analysis of the BTC proposal

Action: for information

7.5. Cooperation with international regulators

7.5.1. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan)

CAT: Martina Schuessler-Lenz

Scope: Agenda of the teleconference of 20 October 2022

Action: for information

7.5.2. WHO approach towards the development of a global regulatory framework for cell and gene therapy products

CAT: Ilona Reischl

Scope: Comments from the public consultation

Action: for information

7.6. CAT work plan

7.6.1. CAT Workplan for 2023

CAT: Martina Schüssler-Lenz

Scope: first reflections on CAT workplan topics for 2023

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Adeno-associated viral (AAV) vector toxicities: regulatory considerations

CAT: Carla Herberts, Egbert Flory

Scope: Discussion paper on insertional mutagenesis and follow-up for AAV gene therapy

Action: for adoption

7.8.2. DARWIN EU Coordination Centre

Scope: Follow up on real world evidence (RWE) and DARWIN EU® and the recently selected data partners and year 1 RWE studies.

Action: for discussion

7.8.3. Update on Clinical Trials Raw Data pilot

Scope: Presentation of the clinical trial raw data pilot

Action: for information

Note: The pilot aims to assess the benefits and practicalities of access to raw data in the assessment of medicines. The pilot, expected to last up to two years, will include 10 regulatory procedures submitted to EMA from September 2022. Recent developments around EMA's raw data pilot and next steps will be presented.

7.8.4. EMA Pilot – enhanced support to academic and non-profit ATMP developers

EMA: Ana Hidalgo

Scope: question and answer on the pilot

Action: for discussion

Note: EMA web announcement (29.09.2022)

EMA pilot offers enhanced support to academic and non-profit developers of advanced therapy medicinal products | European Medicines Agency (europa.eu)

8. Any other business

No items

Date of next CAT meeting:

03-04/11/2022

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

MNAT: Multinational assessment team

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

QRD: Quality review of documents

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: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

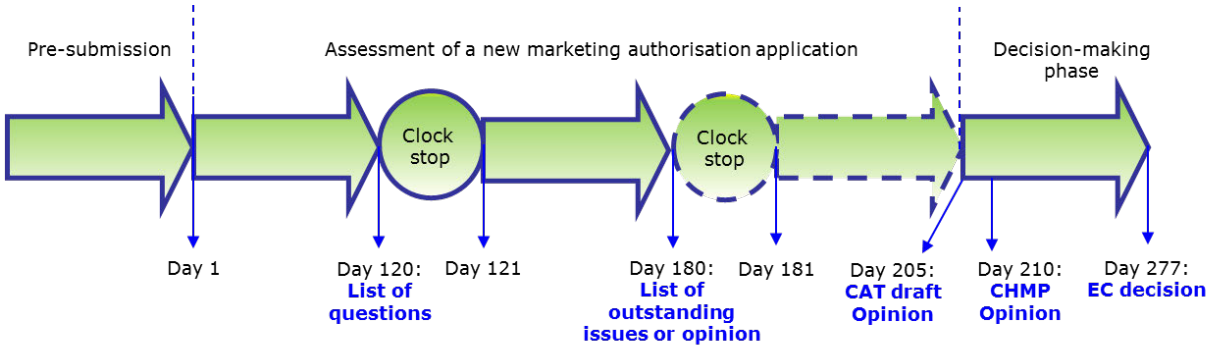
Evaluation of ATMPs (section 2)

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/