14 February 2024
EMA/CAT/39852/2024
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 14-16 February 2024

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

14 February 2024, 14:00 – 18:30, room 1C

15 February 2024, 09:00 – 18:30, room 1C

16 February 2024, 09:00 – 13:00, room 1C

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 14-16 February 2024. See February 2024 CAT minutes (to be published post March 2024 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 14-16 February 2024 meeting

1.3. Adoption of the minutes

CAT minutes for 17-20 January 2024 meeting

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Beremagene geperpavec - PRIME - Orphan - EMEA/H/C/006330

Krystal Biotech Netherlands B.V.; Treatment of patients from birth with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene

Scope: Day 80 assessment report

Action: for information

2.6. Update on ongoing initial applications

No items

2.7. New applications

No items

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. Companion diagnostics

2.10.1. Initial consultation

No items

2.10.2. Follow-up consultation

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/0032

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 08.12.2023.

2.11.2. Breyanzi - Lisocabtagene maraleucel / Lisocabtagene maraleucel - EMEA/H/C/004731/II/0036/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Clinical, RSI

Grouped application comprising two variations as follows:
C.I.4 – Update of sections 4.4 and 4.8 of the SmPC in order to add immune effector cell-associated neurotoxicity syndrome (ICANS) as an adverse drug reaction (ADR) based on the cumulative review of MAH safety database and literature. The Package Leaflet is updated accordingly. In addition, the MAH took this opportunity to introduce editorial changes.
A.6 – To include the ATC Code L01XL08 in section 5.1 of the SmPC.

Action: for adoption

2.11.3. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0021

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays

Scope: Clinical, opinion

Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 1 prior therapy, including an IMiD and a PI, have demonstrated disease progression on or after the last therapy and are refractory to lenalidomide for CARVYKTI, based on interim results from study MMY3002 listed as a specific obligation (SOB/006) in the Annex II. This is an ongoing, Phase 3, randomized, open-label, multicentre study to determine whether treatment with cilta-cel provides an efficacy benefit compared to standard therapy in participants with relapsed and lenalidomide-refractory multiple myeloma. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II of the PI. As part of the application the MAH is requesting a 1-year extension of the market protection.

Action: for adoption

Request for supplementary information adopted on 08.12.2023, 08.09.2023.

2.11.4. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0071

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical, Opinion

Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study CCTL019B2202 (a phase II, single arm, multicentre trial to determine the efficacy and safety of CTL019 in paediatric patients with relapsed and refractory B-cell acute lymphoblastic leukaemia). Submission of cellular kinetic

report for the B-cell acute lymphoblastic leukaemia (ALL) indication based on data from pivotal study CCTL019B2202 and the supportive study CCTL019B2205J involving paediatric ALL patients (partially fulfil REC).
In addition, the MAH took this opportunity to introduce editorial changes.

Action: for adoption

Request for supplementary information adopted on 31.10.2023.

2.11.5. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0075

Novartis Europharm Limited

Rapporteur: Rune Kjeken, PRAC Rapporteur: Gabriele Maurer

Scope: Clinical, opinion

Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study CCTL019C2201 PAES in the Annex II (ANX008); this is a Phase II, single arm, multicentre trial to determine the efficacy and safety of CTL019 in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). The RMP version 6 has also been submitted. In addition, the MAH took the opportunity to update Annex II.D of the PI.

Action: for adoption

Request for supplementary information adopted on 31.10.2023.

2.11.6. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0079/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality, opinion

Action: for adoption

2.11.7. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0013

PTC Therapeutics International Limited

Rapporteur: Joseph DeCourcey

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 19.01.2024, 08.09.2023.

2.11.8. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2500

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, RSI

Action: for adoption

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/017.1

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, RSI

Action: for adoption

2.13.2. Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/REC/018.1

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, fulfilled

Action: for adoption

2.13.3. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/S/0017

PTC Therapeutics International Limited

Rapporteur: Joseph DeCourcey

Scope: Annual Re-assessment, opinion

Action: for adoption

Request for supplementary information adopted on 08.12.2023.

2.13.4. Zolgensma - Onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/P46/022

Novartis Europharm Limited

Rapporteur: Emmely de Vries

Scope: Clinical, RSI

Paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Final study report COAV101A12306: Phase IIIb, open-label, single-arm, single-dose, multicentre study evaluating the safety, tolerability, and efficacy of gene replacement therapy with intravenous OAV101 (AVXS-101) in paediatric patients with spinal

muscular atrophy (SMA).

Action: for adoption

2.13.5. Luxturna - Voretigene neparvovec - EMEA/H/C/PSUSA/00010742/202307

Novartis Europharm Limited

Rapporteur: Gabriele Maurer

Scope: PRAC recommendation

Action: for adoption

2.14. GMP and GCP inspections requests

No items

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:	19.02.2024
-EMA Coordinator's draft report:	01.03.2024
-CAT Coordinator's comments:	06.03.2024
-Revised scientific recommendation:	08.03.2024
-CAT's discussion of scientific recommendation:	15.03.2024

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic human induced pluripotent stem cells-derived corneal limbal stem cells

For treatment of limbal stem cell deficiency

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Olfactory glial cells isolated from autologous human alfactory bulb, expanded in culture

For treatment of complete spinal cord injuries

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Circular RNA capable to bind to mutated regions of the messenger RNA from the DMPK gene

For treatment of myotonic dystrophy type 1

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Modified measles vaccine virus

For the treatment of solid cancer tumours

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. Allogeneic expanded natural killer cells

For the treatment of acute myeloid leukaemia

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. Autologous tissue generated in the human body (in vivo) through the foreign body reaction

For tissue augmentation

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. Dendritic cells activated by lysate of circulating tumour cells

For the treatment of solid tumours in metastatic stage

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.4. Autologous T Lymphocytes engineered with nanoparticles with curcumin incapsulated

For the treatment of melanoma

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.5. Spermatogonial stem cells, propagated *in vitro*

Male infertility due to gonadotoxic treatment

Scope: Procedure on hold pending input/comments from the European Commission

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

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

Timetable:

- Start of procedure at SAWP:	05-08.02.2024
- Appointment of CAT Peer Reviewers:	14-16.02.2024
- SAWP first reports:	26.02.2024
- CAT Peer Reviewer comments (NC/C):	01.03.2024
- CAT Peer Reviewer comments (Q):	06.02.2024
- Discussion at SAWP:	04-07.03.2024
- Discussion at CAT and feedback to SAWP:	13-15.03.2024

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	04-07.03.2024
- Appointment of CAT Peer Reviewers:	13-15.03.2024
- SAWP first reports:	02.04.2024
- CAT Peer Reviewer comments (NC/C):	05.04.2024
- CAT Peer Reviewer comments (Q):	10.04.2024
- Discussion at SAWP:	08-11.04.2024
- Discussion at CAT and feedback to SAWP:	17-19.04.2024

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

6.2.1. Overview of ITF activities in 2023

ITF Coordinator: Oriane Blanquie

Scope: Summary of main activities conducted by ITF in 2023

Action: for information

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	05-08.02.2024
SAWP recommendation:	07.03.2024
CAT recommendation:	15.03.2024
CHMP adoption of report and final recommendation:	21.03.2024

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. CAT membership

Action: for information

7.1.2. Vote by proxy

Action: for information

7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Belgian presidency – 15-17 May 2024

CAT: Claire Beuneu

Scope: Draft agenda of the upcoming SRLM

Action: for discussion

7.1.4. CAT Strategic Review & Learning meeting (SRLM) under the Spanish presidency – 26-27 October 2023

CAT: Sol Ruiz, Marcos Timon

Scope: Final minutes of the SRLM meeting

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. Minutes and draft agenda - PCWP and HCPWP meetings

Scope: Minutes and draft agenda for the PCWP and HCPWP meetings

Action: for information

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

7.3.1. ATMP Quality assessment support group

Scope: To inform the CAT members on the creation of the group of ATMP Quality experts to be contacted to give informal advice and act as sounding board for member states in relation to assessment of quality aspects of ATMPs

Action: for information

7.3.2. Launch of Call for Nominations to Biological Quality PCW

Scope: Mandate and rules of procedure

Action: for adoption

7.4. Cooperation with the EU regulatory network

No items

7.5. Cooperation with international regulators

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

CAT: Ilona Reischl

Scope: Agenda of the teleconference of 22.02.2024

Action: for information

7.5.2. International Pharmaceutical Regulatory Programme (IPRP) Gene and Cell therapy working group

CAT: Pille Säälik

Scope: Agenda of the teleconference of 27.02.2024

Action: for information

7.6. CAT work plan

7.6.1. Guideline on quality, non-clinical and clinical requirements for investigational ATMPs in clinical trials

CAT: Ilona Reischl

Scope: Draft guideline, updated following the external consultation

Action: for adoption for release for external consultation

7.6.2. CAT Scientific symposium, 8-9 October 2024

CAT Chair: Ilona Reischl

Scope: draft programme

Action: for discussion

7.6.3. CAT - regulatory session at the European Society of Gene & Cell Therapy (ESGCT) 2024 meeting

CAT Chair: Ilona Reischl

Scope: To discuss topics on CAT and EMA activities to support developers, progress and challenges in ATMP development for CAT session on ATMP regulatory aspects at the ESGCT meeting that takes place on 22-25 October 2024 in Rome, Italy

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Report from Group for Internal Rules on Extensions of Clock Stops

CAT: Olga Kholmanskikh

Scope: Report on outcomes and proposals to the CHMP. Comments to be sent by 29 February 2024

Action: for discussion

7.8.2. ATMP Support Pilot for academia

Scope: Update and information on selected candidates

Action: for information

7.8.3. CoGenT (Collaboration on Gene Therapies) Pilot

Scope: Internal collaboration of regulatory authorities to facilitate the development of gene therapies for orphan diseases

Action: for information

7.8.4. International Society for cell and gene therapy (ISCT) Annual meeting

CAT: Ilona Reischl

Scope: Invitation to attend the 2nd Annual Global Regulators Summit (28 May 2024) and the panel discussion on Regulatory Considerations for Platform-based Cell and Gene Therapy (29 May 2024)

Action: for agreement

8. Any other business

8.1.1. IRIS training

Scope: Training on the use of IRIS and the new implementation of communication process between CAT Secretariat and Committee participants

Action: for information

Date of next CAT meeting:

13-15 March 2024

9. Explanatory notes

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

For a list of acronyms and abbreviations, see:

List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in relation to EMA's regulatory activities

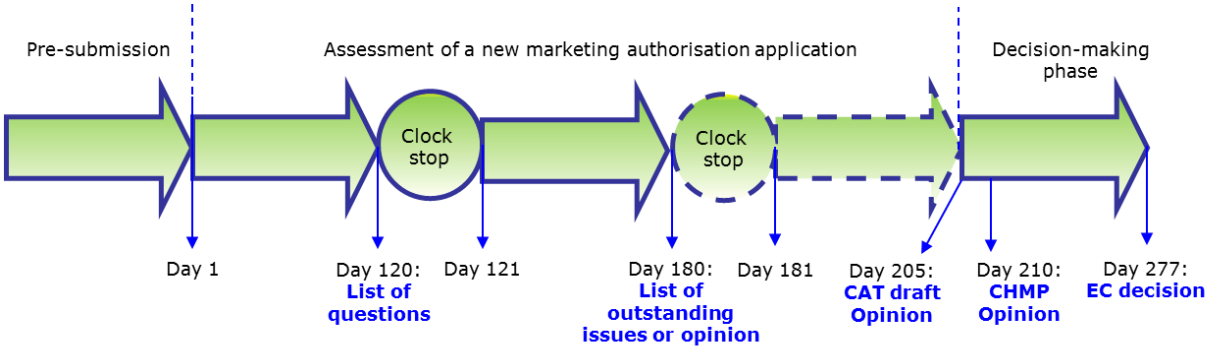
Evaluation of ATMPs (section 2)

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 Post-authorisation activities (section 2.11-2.13) and any ATMP related inspection requests (section 2.14).

New applications (sections 2.1. to 2.9.)

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 2.4) 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 2.3). Section 2.6 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.

New applications (section 2.7.)

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.

Withdrawal of applications (section 2.8.)

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.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.9.)

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.

Companion diagnostics (section 2.10)

This section lists applications for initial and follow-on consultation of companion diagnostics.

Post-authorisation activities (section 2.11-2.13.)

Section 2.11 lists type II variations, including extension of indication applications and re-examination procedures for type II variations for which the applicant has requested re-examination of the opinion previously issued by the CHMP. Section 2.12 list extension application according to Annex I of Reg. 1234/2008 and section 2.13 includes all other post-authorisation activities concerning authorised ATMPs that are not covered elsewhere in the agenda such as post-authorisation measures, 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.

GMP and GCP Inspections Issues (section 2.14.)

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).

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/