20 February 2025
EMA/CAT/62701/2025
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 19-21 February 2025

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

19 February 2025, 14:00 – 18:30, room 0B

20 February 2025, 09:00 – 18:30, room 0B

21 February 2025, 09:00 – 13:00, room 0B

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 19-21 February 2025. See February 2025 CAT minutes (to be published post March 2025 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 19-21 February 2025 meeting

1.3. Adoption of the minutes

CAT minutes for 22-24 January 2025 meeting

2. Evaluation of ATMPs

2.1. Opinions

2.1.1. 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: Opinion

Action: for adoption

List of Outstanding Issues adopted on 06.12.2024 and 11.10.2024. List of Questions adopted on 15.03.2024.

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

No items

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

No items

2.6. Update on ongoing initial applications

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. 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. Abecma - Idecabtagene vicleucel - Orphan - EMEA/H/C/004662/II/0058/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Rune Kjeken

Scope: Quality, request for supplementary information

Action: for adoption

2.11.2. Breyanzi - Lisocabtagene maraleucel / Lisocabtagene maraleucel - EMEA/H/C/004731/II/0055/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, request for supplementary information

Action: for adoption

2.11.3. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0036

Janssen-Cilag International NV

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

Scope: Clinical, request for supplementary information

Update of sections 4.8, and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs), and update clinical efficacy and safety information based on second interim analysis from study 68284528MMY3002 (CARTITUDE-4); this is a phase 3 randomised study comparing ciltacabtagene autoleucel, a chimeric antigen receptor T cell (CAR-T) therapy directed against B cell maturation antigen (BCMA), versus pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd) in subjects with relapsed and lenalidomide-refractory multiple myeloma. The RMP version 5.3 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

Action: for adoption

2.11.4. CARVYKTI - Ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0037

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

2.11.5. Casgevy - Exagamglogene autotemcel - Orphan - EMEA/H/C/005763/II/0009/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 06.12.2024.

2.11.6. Casgevy - Exagamglogene autotemcel - Orphan - EMEA/H/C/005763/II/0012/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

2.11.7. Kymriah - Tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0086/G

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Safety, opinion

A grouped application consisting of:

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on cytokine release syndrome based on literature.

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on neurological adverse reaction based on literature. The Package Leaflet is updated accordingly.

C.I.4: Update of section 4.4 of the SmPC in order to amend existing warnings on hypersensitivity reactions based on post marketing data and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the product information (PI).

Action: for adoption

Request for Supplementary Information adopted on 06.12.2024, 11.10.2024.

2.11.8. Libmeldy - Atidarsagene autotemcel - Orphan - EMEA/H/C/005321/II/0031/G

Orchard Therapeutics (Netherlands) B.V.

Rapporteur: Emmely de Vries

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 08.11.2024.

2.11.9. ROCTAVIAN - Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/II/0014

BioMarin International Limited

Rapporteur: Violaine Closson Carella; PRAC Rapporteur: Bianca Mulder

Scope: Clinical, Opinion

Update of the Annex II in order to propose changes to the current marketing authorisation obligations for Roctavian. The RMP version 1.3 has also been submitted.

Action: for adoption

Request for supplementary information adopted on 08.11.2024.

2.11.10. Yescarta - Axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0085

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical, Request for supplementary information

Submission of the final report from study KT-US-482-0147 (ZUMA-26). This is a prospective, noninterventional, clinical efficacy study investigating and analysing the impact of tumour CD19 antigen expression and density on response to axicabtagene ciloleucel treatment using a quantitative flow cytometry method.

Action: for adoption

2.11.11. Tecartus; Yescarta - Axicabtagene ciloleucel; Brexucabtagene autoleucel - Orphan - EMEA/H/C/WS2736

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, opinion

Action: for adoption

Request for supplementary information adopted on 06.12.2024 and 13.09.2024.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Hemgenix - Etranacogene dezaparvovec - Orphan - EMEA/H/C/004827/REC/009

CSL Behring GmbH

Rapporteur: Silke Dorner

Scope: Quality, REC fulfilled

Action: for adoption

2.13.2. ROCTAVIAN - Valoctocogene roxaparvovec - Orphan - EMEA/H/C/005830/ANX/004.3

BioMarin International Limited

Rapporteur: Violaine Closson Carella

Scope: Clinical

From initial MAA: Annual progress report for study 270-801 (EU PAS 49243; GENEr8-GTR): a retrospective cohort study of patients treated with Roctavian (valoctocogene roxaparvovec).

Action: for adoption

2.13.3. Upstaza - Eladocagene exuparvovec - Orphan - EMEA/H/C/005352/S/0025

PTC Therapeutics International Limited

Rapporteur: Joseph DeCourcey, Co-Rapporteur: Maria Luttgen, PRAC Rapporteur: Gabriele Maurer

Scope: Annual re-assessment

Action: for adoption

Request for supplementary information adopted on 06.12.2024.

2.13.4. Yescarta - Axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/ANX/002.7

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Pharmovigilance

From initial MAA fourth annual interim report for PASS KT-EU-471-0117:
Title: Long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma (EU PAS Register no.: EUPAS32539).

Action: for adoption

2.13.5. Casgevy - Exagamglogene autotemcel - EMEA/H/C/PSA/S/0113

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Blanca Mulder

Scope: Pharmacovigilance

PRAC assessment of substantial amendments to a non-interventional imposed PASS protocol - VX22-290-101 (Version 2.1): Long-term registry-based study of patients with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) treated with exagamglogene autotemcel (exa-cel).

Action: for information

2.14. Companion diagnostics - initial consultation

No items

2.15. Companion diagnostics – Follow-up consultation

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:	21.02.2025
-EMA Coordinator's draft report:	07.03.2025
-CAT Coordinator's comments:	12.03.2025
-Revised scientific recommendation:	14.03.2025
-CAT's discussion of scientific recommendation:	21.03.2025

4.1. New requests – Appointment of CAT Coordinator

4.1.1. mRNA transfected macrophages cultured from autologous monocytes

Treatment of end stage liver disease

Scope: Appointment of CAT coordinator

Action: for adoption

4.1.2. Genetically modified porcine heart

Intended for cardiac xenotransplantation to human patients with end-stage heart failure

Scope: Appointment of CAT coordinator

Action: for adoption

4.1.3. Genetically modified Eschericia coli bacteria engineered to carry genes to metabolize tryptophan and genes to use an exogenously administered sugar source

Treatment of type II diabetes

Scope: Appointment of CAT coordinator

Action: for adoption

4.1.4. mRNAs encoding modified C.acnes protein

Treatment of acne

Scope: Appointment of CAT coordinator

Action: for adoption

4.1.5. Autologous tumour-derived dendritic cells

Prevention of relapse and metastasis of non-small cell lung carcinoma (NSCLC)

Scope: Appointment of CAT coordinator

Action: for adoption

4.1.6. adeno-associated virus (AAV) serotype 1 (AAV1) vector containing the human granulin precursor (GRN) cDNA encoding progranulin (PGRN)

Treatment of frontotemporal dementia (FTD) in adults who have a mutation in the GRN or chromosome 9 open reading frame 72 (C9orf72) genes

Scope: Appointment of CAT coordinator

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

No items

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

No items

4.4. Finalisation of procedure

4.4.1. mRNAs encoding IL-12 and IL-18

Treatment of gastric cancer

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. Autologous Tumour Infiltrating Lymphocytes (TILs)

Treatment of adult patients with advanced or 2/4 metastatic solid tumours who have not responded to standard therapies (chemotherapy, radiation therapy, molecule-targeted therapy) or are ineligible for alternative treatment options or in associated treatment with chemotherapy in multi-model therapy

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. BCMA targeting Chimeric Antigen Receptor expressing mRNA transfected autologous T cells

Treatment of Myasthenia Gravis

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.4. Adeno-associated virus serotype 5 containing the human RORA gene (AAV5-hRORA)

Treatment of adult and paediatric patients with vision loss due to Geographic Atrophy secondary to dry age-related macular degeneration and Stargardt Disease

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

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:	10-13.02.2025
- Appointment of CAT Peer Reviewers:	19-21.02.2025
- SAWP first reports:	03.03.2025
- CAT Peer Reviewer comments (NC/C):	07.03.2025
- CAT Peer Reviewer comments (Q):	12.03.2025
- Discussion at SAWP:	10-13.03.2025
- Discussion at CAT and feedback to SAWP:	19-21.03.2025

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	10-13.03.2025
- Appointment of CAT Peer Reviewers:	19-21.03.2025
- SAWP first reports:	31.03.2025
- CAT Peer Reviewer comments (NC/C):	04.04.2025
- CAT Peer Reviewer comments (Q):	09.04.2025
- Discussion at SAWP:	07-10.04.2025
- Discussion at CAT and feedback to SAWP:	14-16.04.2025

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 2024

Scope: Summary of the main ITF activities and trends in 2024

Action: for information

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	10-13.02.2025
SAWP recommendation:	13.03.2025
CAT recommendation:	21.03.2025
CHMP adoption of report and final recommendation:	27.03.2025

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 Polish presidency

CAT: Dariusz Sladowski

Scope: Preparation for the meeting

Action: for discussion

7.1.4. Committee Meeting Dates for 2027-2028

Scope: Proposed committee meeting dates for the period of 2027-2028

Action: for information

7.1.5. GIREX - Group for Internal Rules on Extensions of Clock Stops

Scope: Update on requests for extensions of clock stops for ongoing procedures

Action: for adoption

7.1.6. Joint CHMP-CAT membership

Scope: Call for expression of interest on the appointment of CHMP members to the CAT

Action: for discussion

7.1.7. Onboarding Programme for CAT members and alternates

CAT: Ilona Reischl

Scope: Onboarding Programme, revision 1

Action: for adoption

7.2. Coordination with EMA Scientific Committees

No items

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

No items

7.4. Cooperation with the EU regulatory network

7.4.1. Update on Real-World Evidence, including DARWIN EU®

Scope: Status of CAR-T cell therapy framework contract study and update about DARWIN EU

Action: for information

7.5. Cooperation with international regulators

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

CAT: Ilona Reischl

Scope: Draft agenda of the teleconference of 27.02.2025

Action: for information

7.6. CAT work plan

7.6.1. Guideline on requirements for investigational ATMPs in clinical trials

CAT: Ilona Reischl

Scope: discussion of the plan of actions for the 2025 work plan topic on the guideline for investigational ATMPs (preparation of a scientific publication on the guideline and the analysis of clinical trials with ATMPs in the EU; organisation of training/webinar on the guideline).

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Draft MHRA guideline on individualised mRNA cancer immunotherapies

CAT: Ilona Reischl

Scope: Draft guideline, published for consultation (deadline 31.03.2025)

Action: for information

Note: Link to the document

7.8.2. Neo-antigen peptide vaccines as magistral preparation?

CAT: Ilona Reischl

Scope: Short feedback from a discussion with FDA

Action: for information

8. Any other business

No items

Date of next CAT meeting:

19-21 March 2025

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

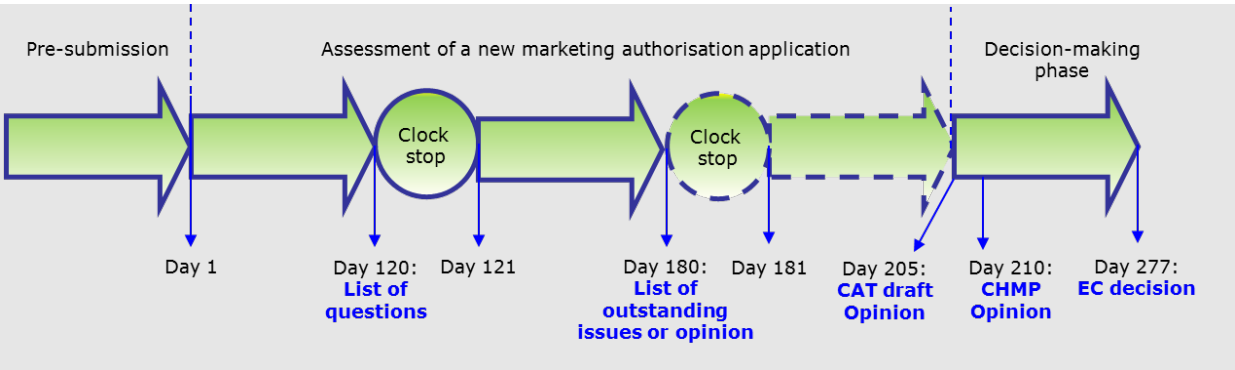
Evaluation of ATMPs (section 2)

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.

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 2.11-2.13.)

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.

Companion diagnostics (section 2.14-2.15)

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

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/