02 December 2020
EMA/CAT/662327/2020
Human Medicines Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 02-04 December 2020

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

02 December 2020, 14:00 – 18:30, virtual meeting

03 December 2020, 09:00 – 18:00, virtual meeting

04 December 2020, 09:00 – 13:00, 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 02-04 December 2020. See December 2020 CAT minutes (to be published post-January 2021 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 02-04 December 2020 meeting

1.3. Adoption of the minutes

CAT minutes for 04-06 November 2020 meeting

2. Evaluation of ATMPs

2.1. Opinions

No items

2.2. Oral explanations

No items

2.3. Day 180 list of outstanding issues

2.3.1. Idecabtagene vicleucel - Orphan - EMEA/H/C/004662

Accelerated assessment

Celgene Europe BV; treatment of multiple myeloma

Scope: Day 180 List of outstanding issues

Action: for adoption

List of Questions adopted on 11.09.2020.

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Elivaldogene autotemcel - Orphan - EMEA/H/C/003690

Accelerated assessment

bluebird bio (Netherlands) B.V; treatment of patients less than 18 years of age with an *ABCD1* genetic mutation and early cerebral adrenoleukodystrophy

Scope: feedback on ongoing assessment

Action: for information

2.6. Update on ongoing initial applications

No items

2.7. New applications

2.7.1. Lenadogene nolparvovec – Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of Leber Hereditary Optic Neuropathy

Scope: timetable for assessment

Action: for adoption

2.8. Withdrawal of initial marketing authorisation application

2.8.1. Autologous human chondrocytes in vitro expanded - EMEA/H/C/004598

Repair of cartilage defects of the knee joint

Scope: letter dated 19.11.20. from the applicant withdrawing the marketing authorisation application (MAA).

Action: for information

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. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0027

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality:

Action: for adoption

Request for Supplementary Information adopted on 06.11.2020, 09.10.2020.

2.11.2. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0008

Novartis Gene Therapies EU Limited

Rapporteur: Hans OvelgönneScope: Clinical: Update to SmPC for sections 4.4 (Special warnings and precautions for use), 4.8 (Undesirable Effects) and corresponding sections in the Package Leaflet to add a new safety signal of 'Thrombotic microangiopathy'.
Action: for adoption

2.11.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0009/G

Novartis Gene Therapies EU Limited

Rapporteur: Hans OvelgönneScope: Quality

Action: for adoption

2.11.4. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/C/003691/II/0017

bluebird bio (Netherlands) B.V

Rapporteur: Carla HerbertsScope: Quality

Action: for adoption

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. Strimvelis – autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - Orphan - EMEA/H/C/003854

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruíz; PRAC: Menno van der Elst

Scope: safety: report of a serious adverse event (lymphoid T cell leukaemia) potentially related to an insertional mutagenesis event

Action: for discussion

2.13.2. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/REC/015

Novartis Gene Therapies EU Limited

Rapporteur: Hans Ovelgönne, CHMP Coordinator: Johann Lodewijk Hillege

Scope: Letter of Recommendation.

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:	21.12.2020
-Draft CAT co-ordinator's report:	08.01.2021
-ITF peer-review comments:	13.01.2021
-Revised scientific recommendation:	15.01.2021
-Adoption of scientific recommendation by CAT:	22.01.2021

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Autologous bone marrow aspirate concentrate

Intended for the repair mechanism for bone repair in a variety of bony defects such as fractures, arthroplasty, bone cysts, osteonecrosis, or avascular necrosis

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. *In vitro* expanded autologous human articular chondrocytes

Intended for the repair of symptomatic, localised, full-thickness cartilage defects of the knee joint in patients with closed epiphyseal growth plates.

Scope: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous bone marrow derived mesenchymal stem cells (amyotrophic lateral sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

4.2.2. Autologous bone marrow derived mesenchymal stem cells (multiple sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

4.2.3. Autologous anti-CD19 chimeric antigen receptor T cells

Intended for the treatment of B- cell malignancies

Scope: ATMP scientific recommendation

Action: for adoption

4.2.4. Autologous omental adipose tissue and biodegradable fibrin glue

Intended for the treatment of renal traumatic/disease conditions

Scope: ATMP scientific recommendation

Action: for adoption

4.2.5. Messenger ribonucleic acid (mRNA) encoding the human glucose debranching enzyme (GDE)

Intended for the treatment of glycogen storage disease III

Scope: ATMP scientific recommendation

Action: for adoption

4.2.6. *In vitro* transcribed messenger ribonucleic acid (mRNA) encoding human interleukin 2 (IL-2), linked to interfering RNA targeting vascular endothelial growth factor A (VEGF-A)

Intended for the treatment of solid tumours

Scope: ATMP scientific recommendation

Action: for adoption

4.2.7. Wharton's jelly derived mesenchymal stem cells (WJ-MSCs) (multiple sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

4.2.8. Wharton's jelly derived mesenchymal stem cells (WJ-MSCs) (amyotrophic lateral sclerosis)

Intended for the treatment of amyotrophic lateral sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

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

No items

4.4. Finalisation of procedure

4.4.1. Autologous CD34+ cells transduced with a lentiviral vector encoding human cystinosin

Intended for the treatment of cystinosis

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

Action: for information

4.4.2. 3D bio-printed bionic pancreas composed of islets of Langerhans and non-viable printable porcine-derived matrix plus porcine–derived decellularised blood vessel – H0005801

Intended for the treatment of late-chronic pancreatitis

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

Action: for information

4.4.3. 3D bio-printed bionic pancreas composed of insulin- and glucagon-releasing cells and non-viable printable porcine-derived matrix plus porcine–derived decellularised blood vessel – H0005802

Intended for the treatment of brittle diabetes mellitus type I

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

Action: for information

4.4.4. Autologous tumour-infiltrating lymphocytes

Intended for the treatment of advance melanoma

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

Action: for information

4.4.5. Delolimogene mupadenorepvec (oncolytic adenovirus expressing two immunostimulatory transgenes (TMZ-CD40L and 4-1BBL))

Intended for the treatment of cancer

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

Action: for information

4.4.6. Allogeneic cord tissue-derived mesenchymal stromal cells

Intended for the treatment of inflammatory and immunological diseases (acute graft-versus-host disease, systemic lupus erythematosus, systemic sclerosis, acute respiratory distress syndrome)

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

Action: for information

4.5. Follow-up and guidance

No items

5. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

5.1. New requests – appointment of CAT Rapporteurs

Timetable:
-Final Briefing Package: 07.12.2020
-Start of the procedure at SAWP: 11-14.01.2021
-CAT report due by: 15.01.2021
-CAT recommendation: 22.01.2021

5.2. CAT reports

5.3. List of Issues

No items

5.4. Finalisation of SA procedures

6. Pre-Authorisation Activities

Information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

6.1. Paediatric investigation plans

No items

6.2. ITF briefing meetings in the field of ATMPs

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	26.11.2020
SAWP recommendation:	14.01.2021
CAT recommendation:	22.01.2021
CHMP adoption of report and final recommendation:	28.01.2021

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

France: Nathalie Morgensztejn - membership mandate (alternate) ended on 12 November 2020

Action: for information

7.1.2. Joint CHMP-CAT memberships

Scope: Joint CHMP-CAT membership, new mandate 2020-2023 for: Romaldas Mačiulaitis, Sol Ruíz, Bruno Sepodes, Jan Mueller-Berghaus and John Borg

Action: appointment of alternate to Sol Ruiz and Jan Mueller-Berghaus

7.1.3. Accelerated assessment – update of the AA tool

Scope: presentation of the new template and review of the accelerated assessment tool for ATMPs and non-ATMPs

Action: for discussion

7.1.4. Revision of the ATMP classification procedure

Scope: presentation of new procedure

Action: for information

7.2. Coordination with EMA Scientific Committees

No items

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

7.3.1. EMA – Review of Working Parties

CAT: Martina Schüssler-Lenz

Scope: feedback from the SciCoBo meeting that took place on 30 November 2020 on the review of activities of the working parties of the EMA

Action: for information

7.3.2. Correspondence with Alliance for Regenerative Medicine (ARM) on the use of master files and certification schemes for ATMP manufacturing in Europe

CAT: Sol Ruíz

Scope: Response from EMA/CAT to ARM on the use of master files and certification schemes for ATMP manufacturing in Europe

Action: for discussion

Note: this topic was discussed previously in in BWP in June 2020 and CAT in July 2020

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

CAT: Martina Schüssler-Lenz

Scope: Amendment to section 6.5 (Clinical efficacy) following comments provided by Oncology and Biostatistics Working Party.

Action: for discussion

Note: this guideline was adopted by CAT in October 2020 and CHMP in November 2020. Publication has been put on hold to allow re-discussion of the clinical efficacy section

7.4. Cooperation within the EU regulatory network

7.4.1. Inspection of manufacturers of viral vectors used as starting materials for genetically modified cells

CAT drafting group members: Heli Suila, Ivana Haunerova, Marcos Timón, Violaine Closson Carella

Scope: draft Q&A on principles for GMP

Action: for discussion

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

CAT: Martina Schüssler-Lenz

Scope: inception impact assessment on the revision of the BTC legislation

Action: for discussion

Note: the European Commission has opened the inception impact assessment for feedback by 14 December 2020.
https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12734-Revision-of-the-Union-legislation-on-blood-tissues-and-cells-

7.4.3. Heads of Medicines Agencies (HMA)-EMA joint big data – Big data training signpost

Action: for discussion

Note: the Big Data training signpost is a collection of external training courses on Big Data skills that we believe can benefit the network until the Big Data curriculum is ready which will contain tailor-made and more targeted trainings instead.

7.4.4. Multi-stakeholder webinar to support implementation of the Medical Devices Regulation on drug-device combinations

CAT: Ilona Reischl

Scope: feedback from the workshop and implications for ATMPs

Action: for discussion

Note: information on the multistakeholder webinar can be found here:
https://www.ema.europa.eu/en/events/multi-stakeholder-webinar-support-implementation-medical-devices-regulation-drug-device-combinations

7.4.5. Regulatory status of RNA products

CAT: Marcos Timón, Violaine Closson-Carella, Egbert Flory, Hans Ovelgönne

Scope: reflection on the consequences for ATMPs of the Commission's feedback on the regulatory status of RNA products in the context of vaccines against COVID-19

Action: for discussion

Note: further to a discussion in July 2020 (see CAT minutes of the July CAT meeting, point 7.4.2), a brainstorming meeting took place (between CAT secretariat and CAT members) to reflect upon the consequence for the ATMP field of the Commission's feedback on a question from EMA on the status of RNA vaccines that are prepared fully synthetically. Feedback from the brainstorming meeting will be provided.

7.5. Cooperation with international regulators

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

CAT: Martina Schüssler-Lenz

Scope: feedback on the teleconference to took place on 12 November 2020

Action: for information

7.5.2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) – ICH-S12 guideline

CAT: Rune Kjeken, Claire Beuneu

Scope: feedback on the development of the ICH-S12 guideline: Nonclinical Biodistribution Studies for Gene Therapy Products

Action: for discussion

7.5.3. International Pharmaceutical Regulators Programme – Gene therapy working group

CAT: Pille Säälik

Scope: feedback from the teleconference that took place on 12 November 2020

Action: for discussion

7.6. CAT work plan

7.6.1. CAT work plan 2021

Scope: draft CAT work plan 2021

Action: for discussion

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q4/2020 update of the business pipeline report for the human scientific committees

Action: for information

7.8. Others

7.8.1. Process for documenting of CAT experiences / CAT learning

CAT: Martina Schüssler Lenz, Niamh Curran, Carla Herberts, Heli Suila

Scope: Process for collecting and maintaining CAT learnings and presentation of CAT learnings: ‘

Action: for discussion

8. Any other business

No items

Date of next CAT meeting:

20-22/01/2021

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: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

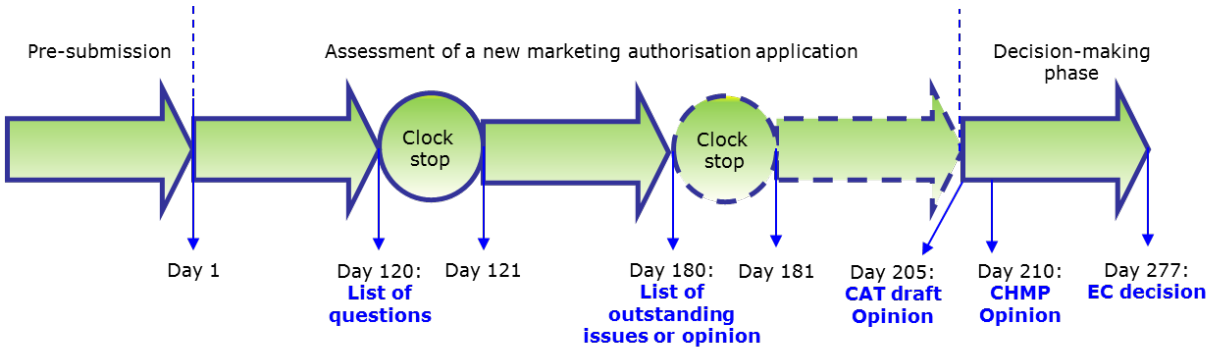
Evaluation of ATMPs (section 2)

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/