4 October 2023
EMA/CAT/419753/2023
Human Medicines Division

Committee for Advanced Therapies (CAT)

Draft agenda for the meeting on 04-06 October 2023

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

04 October 2023, 14:00 – 18:30,

05 October 2023, 09:00 – 18:30,

06 October 2023, 09:00 – 13:00,

Webex: https://ema-europa.webex.com

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 04-06 October 2023. See October 2023 CAT minutes (to be published post November 2023 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 04-06 October 2023 meeting

1.3. Adoption of the minutes

CAT minutes for 06-09 September 2023 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

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. 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/0019

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, opinion

Action: for adoption

Request for Supplementary Information adopted on 16.06.2023.

2.11.2. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0028/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, opinion

Action: for adoption

2.11.3. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0023

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Quality, Request for Supplementary Information

Action: for adoption

2.11.4. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0014/G

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Clinical, request for supplementary information

Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update information on safety and efficacy, based on final results from studies NTUH-AADC-010 and NTUH-AADC-011. NTUH-AADC-010 is an open-label, single arm, externally controlled trial to evaluate safety, efficacy, pharmacodynamics and immunogenicity of AGIL-AADC in children from 18 months to less than 18 years of age with severe aromatic L-amino acid decarboxylase (AADC) deficiency, while NTUH-AADC-011 is an open-label, single arm, externally controlled trial to evaluate efficacy and safety of AGIL-AADC in children from 18 months to less than 6 years of age with severe AADC deficiency. In addition, sections 4.5, 4.9 and 6.6 of the SmPC are updated in order to provide better clarification and guidance for the medical practice. The Package Leaflet is updated accordingly. The MAH also took the opportunity to update the due date of the final report of study AADC-1602 in the Annex II, considering the 10-year follow up of the last patient in study AADC-011, and to introduce minor editorial changes to the product information (PI).

Action: for adoption

2.11.5. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0063

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus

Scope: Clinical, opinion

Update of section 5.1 of the SmPC in order to include new clinical data based on Overall Survival (OS) Primary Analysis from study KTE-C19-107 (ZUMA-7); this is a phase 3, randomised, open-label study evaluating the efficacy of axicabtagene ciloleucel versus standard of care therapy in subjects with relapsed/refractory diffuse large B cell lymphoma (DLBCL) in the 2nd line setting. In addition, the MAH took the opportunity to submit a consolidated Environmental Risk Assessment (ERA) document.

Action: for adoption

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/015

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, Request for supplementary information

Action: for adoption

2.13.2. Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - Orphan - EMEA/H/C/002450/R/0058

Holostem Terapie Avanzate s.r.l.

Rapporteur: Egbert Flory, Co-Rapporteur: Concetta Quintarelli, PRAC Rapporteur: Rhea Fitzgerald

Scope: 1 year Renewal of Marketing Authorisation, request for supplementary information

Action: for adoption

2.13.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/009.6

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Pharmacovigilance, request for supplementary information

From Initial MAA:
Study CCTL019H2301:
Post-authorisation efficacy study (PAES):
In order to further characterise the long-term efficacy and safety of Kymriah in relapsed/refractory Diffuse large B cell lymphoma (DLBCL), the applicant should submit the final overall survival results of study CCTL019H2301 – open-label, Phase III study of Kymriah versus standard of care in adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma.
PROTOCOL VERSION 4

Action: for adoption

2.13.4. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/REC/009

Orchard Therapeutics (Netherlands) B.V.

Rapporteur: Johannes Hendrikus Ovelgonne

Scope: Quality, opinion

Action: for adoption

2.13.5. Tecartus - brexucabtagene autoleucel - EMEA/H/C/005102/R/0034

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-rapporteur: Rune Kjeken, PRAC Rapporteur: Menno van der Elst

Scope: Annual Renewal (with RMP)

Action: for adoption

2.13.6. Hemgenix - etranacogene dezaparvovec - EMEA/H/C/4827/R/0007

CSL Behring GmbH

Rapporteur: Silke Dorner, PRAC Rapporteur: Menno van der Elst

Scope: Annual Renewal

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:	10.10.2023
-EMA Coordinator's draft report:	20.10.2023
-CAT Coordinator's comments:	24.10.2023
-Revised scientific recommendation:	25.10.2023
-CAT's discussion of scientific recommendation:	31.10.2023

4.1. New requests – Appointment of CAT Coordinator

4.1.1. Allogeneic peripheral blood-derived HSPC, Treg cells and Tcon cells

Prevention of moderate to severe chronic graft-vs.-host disease and/or death in patients with acute leukaemias and in patients with myelodysplastic syndrome (MDS) undergoing HLA-matched allogeneic hematopoietic stem cell transplant (alloHCT)

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.2. Spermatogonial stem cells, propagated *in vitro*

Male infertility due to gonadotoxic treatment

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.3. Live, freeze-dried, genetically modified Lactococcus lactis strain, engineered to secrete human interleukin-10 (hIL-10) and a deamidated, human leukocyte antigen (HLA)-DQ2 restricted, 33-mer alpha-gliadin peptide (dDQ2)

Treatment of celiac disease

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.4. Autologous lymphocytes enriched in activated natural killer cells

Cancer

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.5. Umbilical cord blood leukocyte concentrate containing cord blood stem cells

Hypoxic-ischaemic encephalopathy

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.6. Umbilical cord blood leukocyte concentrate containing cord blood stem cells

Cerebral palsy

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.7. DNA plasmid expressing short hairpin RNA (shRNA) against lytic origin of DNA replication of Epstein Barr Virus (EBV) messenger RNA (mRNA)

Treatment of EBV infected patients

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.1.8. DNA plasmid expressing short hairpin RNA (shRNA) against BCL2 anti-apoptotic messenger RNA (mRNA)

Treatment of cancer patients

Scope: Appointment of CAT Coordinator and adoption of timetable

Action: for adoption

4.2. Day 30 ATMP scientific recommendation

4.2.1. Devitalised cell-derived cartilaginous tissue

Bone substitute for maxillofacial and/or orthopaedic bone defects

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 ex-vivo expanded pluripotent stem cell-derived cardiac ventricular progenitor cells

Intended for the treatment of chronic and acute heart disease

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.2. Allogeneic ex-vivo expanded pluripotent stem cell-derived photoreceptor progenitor cells

Intended for the treatment of retinitis pigmentosa

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.3. Allogeneic genetically modified human induced pluripotent stem cell-derived retinal pigment epithelial cells

Intended for the treatment of Stargardt indication

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.4. Autologous cultured fibroblasts

Intended for the treatment of scars and wounds

Scope: European Commission raised no comments. ATMP scientific recommendation

Action: for adoption

4.4.5. Secretome (conditioned medium) from donor bone marrow mesenchymal stem cells (MSCs) containing cytokines, growth factors, proteins and extracellular vesicles

Intended for the treatment of paediatric respiratory diseases called childhood interstitial lung disease (ChILD)

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:	25-28.09.2023
- Appointment of CAT Peer Reviewers:	04-06.10.2023
- SAWP first reports:	16.10.2023
- CAT Peer Reviewer comments (NC/C)	20.10.2023
- CAT Peer Reviewer comments (Q)	25.10.2023
- Discussion at SAWP:	23-26.10.2023
- Discussion at CAT and feedback to SAWP:	30-31.10.2023

5.1.2. Scientific advice procedures starting at the next SAWP meeting

Timetable:

- Start of procedure at SAWP:	23-26.10.2023
- Appointment of CAT Peer Reviewers:	30-31.10.2023
- SAWP first reports:	20.10.2023
- CAT Peer Reviewer comments (NC/C)	24.11.2023
- CAT Peer Reviewer comments (Q)	29.11.2023
- Discussion at SAWP:	27-30.11.2023
- Discussion at CAT and feedback to SAWP:	06-08.12.2023

No items

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

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

No items

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

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	25-28.10.2023
SAWP recommendation:	26.10.2023
CAT recommendation:	31.10.2023
CHMP adoption of report and final recommendation:	09.11.2023

No items

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 Spanish presidency, 25-27 October 2023 Madrid (Spain)

CAT: Sol Ruiz, Marcos Timon

Scope: Agenda of the upcoming SRLM

Action: for discussion

7.1.4. Onboarding Program for CAT members and alternates

CAT: Ilona Reischl

Scope: Presentation of document and buddy system for new CAT members and alternates

Action: for discussion

7.1.5. Training on IRIS for the use of CAT members

Scope: Training on how CAT members can use IRIS for SA and PRIME reports

Action: for information

7.1.6. Refresher on CAT SAWP interactions

Scope: Refreshing training on roles of CAT Peer Reviewers for SA

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. Frequently asked questions on medicinal products development and assessment involving companion diagnostic (CDx)

CAT: Ilona Reischl

Experts: Joerg Engelbergs, Olga Kholmanskikh

Scope: Update from the Companion Diagnostics Expert Group

Action: for review and endorsement

7.2.2. Update on the interphase with the Medical Device Regulation (MDR)

CAT: Ilona Reischl

Scope: Oral update

Action: for information

7.2.3. EPAR development

Scope: Information in the EPAR in case of withdrawal of the marketing authorisation before opinion

Action: for information

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

No items

7.4. Cooperation with the EU regulatory network

7.4.1. Support to member states for the assessment of ATMP Marketing Authorisation Applications

CAT: Ilona Reischl

Scope: Update following the teleconference regarding the general discussion on needs and start of survey on resources (ATMP assessors) available in the NCAs

Action: for information

7.5. Cooperation with international regulators

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

CAT: Ilona Reischl

Scope: Update of the teleconference that took place on 28.09.2023

Action: for information

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

CAT: Pille Säälik

Scope: Update of the teleconference that took place on 28.09.2023

Action: for information

7.6. CAT work plan

7.6.1. CAT work plan for 2024

CAT: Ilona Reischl

Scope: Brainstorming session on work plan topics for 2024

Action: for discussion

7.6.2. Guideline on quality, non-clinical and clinical requirement for investigational ATMPs in clinical trials

CAT: Ilona Reischl

Scope: Feedback from the drafting group discussion on the introduction, scope and general comments made by the stakeholders

Action: for discussion

7.7. Planning and reporting

No items

7.8. Others

7.8.1. Training of CAT members and assessors

CAT: Marcos Timon

Scope: Training on Guideline on quality, non-clinical and clinical aspects of medicinal

products containing genetically modified cells

Action: for information

8. Any other business

Date of next CAT meeting:

30-31 October 2023

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

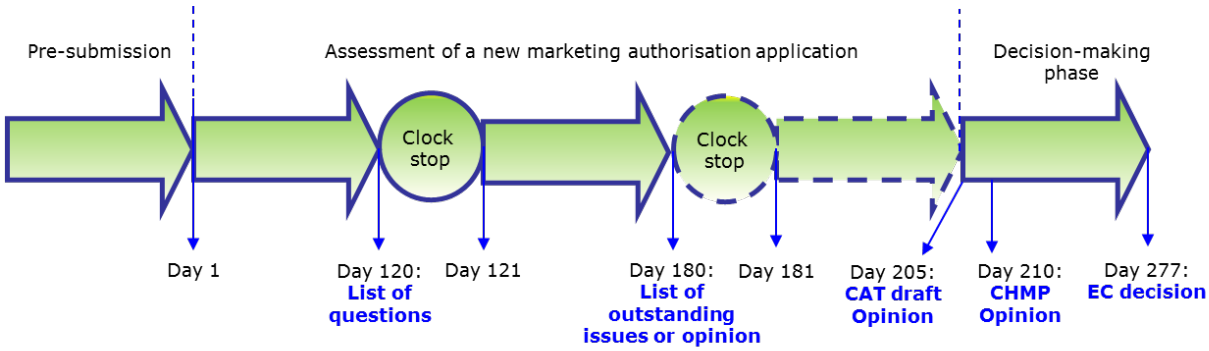
Evaluation of ATMPs (section 2)

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/