17 September 2015
EMA/CAT/629516/2015
Procedure Management and Committees Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 17-18 September 2015

Chair: Paula Salmikangas - Vice-chair: Martina Schüßler-Lenz

17 September 2015, 09:00 – 18:30, room 02-F
18 September 2015, 09:00 – 15:00, room 02-F

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Table of contents

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 17-18 September 2015. See September 2015 CAT minutes (to be published post October 2015 CAT meeting).

1.2. Adoption of agenda

CAT agenda for 17-18 September 2015

1.3. Adoption of the minutes

CAT minutes for 16-17 July 2015

1.4. August Written Procedure

Report of the August 2015 Written Procedure

1.5. Technical information

2. Evaluation of ATMPs

2.1. Opinions

None

2.2. Oral explanations

2.2.1. Talimogene laherparepvec; EMA/H/C/0002771

Treatment of adults with melanoma that is regionally or distantly metastatic

Scope: Oral explanation and report from the SAG oncology

Action: Oral explanation to be held on 17.09.2015 at 17:00hrs

Documents:
SAG report
SAG List of Participants
BWP report

Note:
List of Questions to SAG adopted on 19.06.15
List of Outstanding Issues adopted on 19.06.15
List of Questions adopted on 16.01.15
Classification as a GTMP adopted in July 2012
SAs provided by SAWP in 2008 and 2013

2.3. D180 List of outstanding issues (LoOIs)

None

2.4. D120 Lists of questions (LoQs)

2.4.1. Autologous CD34+ cells transduced with retroviral vector containing the adenosine deaminase gene; *Orphan*; EMA/H/C/003854

GlaxoSmithKline Trading Services- UK; treatment of children aged 0-18 diagnosed with ADA-SCID and for whom no suitable HLA-identical sibling bone marrow donor is available.

Scope: Day 120 list of questions

Action: for adoption

Documents:
BWP report
Integrated Inspection Report (IIR)

Notes:
CAT granted an accelerated assessment in April 2015
Consultation of the Environmental bodies on the Environmental Risk Assessment (GMO)

2.5. Day 80 assessment reports

None

2.6. Re-examination procedure (new applications) under Article 9(2) of Regulation No. 726/2004

2.6.1. Heparesc - allogeneic human heterologous liver cells; *Orphan*; EMA/H/C/003750

Cytonet GmbH & Co. KG; treatment of urea cycle disorders (UCD)Scope: re-examination of the Opinion and consultation of SAG**Action:** for adoption

Documents:
Draft List of Questions to the ad hoc expert group
Preliminary List of Experts for endorsement by CAT

Ad-hoc expert group expertise required:
-Paediatrician and/or paediatric intensive care specialist with expertise in urea cycle disorders
-Paediatrician hepatologist with expertise in liver genetic diseases
-Surgeon with expertise in paediatric liver surgery
-Preclinical lab specialist with expertise in urea cycle disorders

Nominations of experts should be sent by 22 September 2015

The ad hoc expert group meeting will take place on Tuesday 6 October 2015.

Note:
The CAT adopted in April 2015 a negative draft Opinion.
The CHMP adopted in June 2015 a negative Opinion.

2.7. Withdrawal of initial full application

None

2.8. Ongoing initial full application

None

2.9. New applications

2.9.1. Expanded adipose-derived stem cells of allogeneic origin – eASCs; *Orphan*; EMA/H/C/0004258

TiGenix S.A.U.; Intended for the treatment of complex perianal fistulas in adult patients

Scope: Rapporteurship & Peer reviewers nominations

Action: for information

Note:
The CHMP granted at its June 2015 plenary eligibility as a centralised product under Art. 3(1) Indent 1a ATMP Regulation (EC) 126/2004

2.10. GMP and GCP inspections requests

None

2.11. Type II variations

2.11.1. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/34

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey
Scope: submission of final study report CT-AMT—011-02

Action: for adoption

Opinion

2.11.2. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/37-G

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Scope: PI update section 4.8 and 5.1 (five years FU of final CSR study 011.01) and FU of 011.3

Action: for adoption

Opinion

2.11.3. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/38

UniQure Biopharma B.V.;

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey
Scope: PI update sections 5.1 (final CSR study 011.05) (FU of 011.03)

Action: for adoption

Opinion or RSI

2.11.4. Glybera – alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/46-G

UniQure Biopharma B.V.;

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey
Scope: changes to manufacturing process of the active substance (grouped variation) to introduce a viral clearance nanofiltration step.

Action: for adoption

Opinion or RSI

2.12. Other post-authorisation activities

2.12.1. Holoclar – *ex vivo* expanded autologous human corneal epithelial cells containing stem cells; *Orphan*; EMA/H/C/002450/R/0001

Chiesi Farmaceutici S.p.A.; treatment of adult patients with moderate to severe limbal stem cell deficiency

Rapporteur: E. Flory, CAT Co-Rapporteur: P. Gasparini; CHMP Coordinator: J. Mueller-Berghaus
Scope: Conditional Renewal

Action: Timetable for silent adoption

Note: conditional MA adopted in December 2014

2.12.2. ChondroCelect – characterised viable autologous cartilage cells expanded in vivo expressing specific marker proteins; EMA/H/C/00878/MEA 16.4. 18.4

TiGenix N.V.;

Scope 16.4: randomised control trial protocol TIG/ACT/04/2009
Scope 18.4: Non-interventional Registry of ChondroCelect, Study TGX001-2011 & Randomised Controlled Study in small lesions using microfracture as comparator

Rapporteur: Egbert Flory; Co-rapporteur: Tiina Palomäki; CHMP Coordinators: Jan Müller-Berghaus

Action: for information

3. Certification of ATMPs

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

3.1. New applications

3.2. Day 60 evaluation reports

None

3.3. Opinions

None

4. Scientific Recommendation on Classification of ATMPs

4.1. New requests – appointment of CAT Co-ordinators

4.1.1. Allogeneic mesenchymal precursor cells

Intended for the treatment of chronic lumbar back pain

Scope: adoption of TT and appointment of CAT Co-ordinator

Action: for adoption

Request received 20th August 2015

Appointment of CAT Co-ordinator

4.1.2. *In vitro* expanded autologous articular chondrocytes

intended for the treatment of articular cartilage defect

Scope: adoption of TT and appointment of CAT Co-ordinator

Action: for adoption

Request received 18th August 2015

Appointment of CAT Co-ordinator

4.1.3. Autologous cells of stromal vascular fraction (SVF) of adipose tissue

Intended for (1) cosmetic lipofiling; (2) treatment for non-healing wounds and scared tissue; (3) treatment of osteoarthritis in the knee

Scope: adoption of TT and appointment of CAT Co-ordinator

Action: for adoption

Request received 27th August 2015

Appointment of CAT Co-ordinator

4.1.4. Decellularised trachea seeded with autologous expanded MSCs

Intended for the treatment of reconstruction of trachea subsequent to damage or stenosis due to cancer, injury, infection or congenital deformities

Scope: adoption of TT and appointment of CAT Co-ordinator

Action: for adoption

Request received 3rd September 2015

Appointment of CAT Co-ordinator

4.1.5. Autologous mesenchymal stem cells isolated from bone marrow or adipose tissue; allogeneic mesenchymal stem cells from umbilical cord

Intended for the treatment of Amyotrophic Lateral Sclerosis

Scope: adoption of TT and appointment of CAT Co-ordinator

Action: for adoption

Request received 3rd September 2015

Appointment of CAT Co-ordinator

4.2. Day 30 Co-ordinators' first reports

4.2.1. hESC-derived Hepatocyte like cells

Intended for the treatment of inborn errors of liver metabolism diseases and liver acute failure.

Action: for adoption

Classification report

4.2.2. Life-attenuated, double-delete Listeria monocytogenes expressing human mesothelin

Intended for the treatment of malignant pleural mesothelioma.

Action: for adoption

Classification report

4.2.3. Allogeneic hematopoietic progenitor cells (HPC–CD34+) accompanied by facilitating cells (FC– CD8+/αβTCR-) and αβ T cells, prepared from mobilized peripheral blood mononuclear cells.

Intended for the prophylaxis of organ rejection in adult patients receiving living donor kidney transplantation.

Action: for adoption

Classification report

4.2.4. Encapsulated allogeneic cells genetically modified to secrete GM-CSF and irradiated autologous tumour cells

Intended for the treatment of advanced solid tumours.

Action: for adoption

Classification report

4.3. Finalisation of procedures

None

4.4. Follow-ups and guidance

None

5. Scientific Advice

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

5.1. New scientific advices – appointment of CAT Rapporteur

5.2. CAT Rapporteurs' reports

5.3. Lists of issues

5.4. Finalisation of Scientific Advice procedures

6. Pre-Authorisation Activities

Disclosure of 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 (PIP)

6.2. ITF briefing meetings in the field of ATMPs

None

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

Denmark: Sinan B. Sarac - termination of mandate for member

Action: for information

7.1.2. CAT minutes

Scope: Rolling minutes as a working tool for CAT members

Action: for information

7.2. Coordination with EMA Scientific Committees

7.2.1. Committee for Medicinal Products for Human Use (CHMP)

Summary of Outcomes (SoO) for the July 2015 meeting

Action: for information

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

7.3.1. Good Laboratory Practice (GLP) requirements of non-clinical studies for ATMPs

Action: for discussion

Note:
June 2015: presentation by the EMA GLP IWP on GLP requirements for ATMPs
July 2015: CAT agreed on the composition of a drafting group to draft a document summarising experiences and expectation in relation to the GLP requirements of non-clinical studies of ATMP
17-18 September 2015: discussion of the observations made by the CAT drafting group members
15-16 October 2015: joint discussion with the GLP IWP to agree on a common position

7.3.2. Pharmacovigilance: GVP Module P.II Biologicals

Action: for discussion

Document:
Module

Note: this module is presented to committees for discussion and comments before a public consultation

7.3.3. Adaptive pathway approach (formerly known as adaptive licensing)

CAT resources: Hans Ovelgönne

Scope: presentation of the procedure and experience with ATMPs under discussion in the AP

Action: for information

Further information can be found here: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp&mid=WC0b01ac05807d58ce

7.3.4. ADAPT SMART (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes)

EMA resources: Hans-Georg Eichler, EMA's Senior Medical Officer

Action: for information

Further information can be found here:
http://adaptsmart.eu/press-release-innovative-medicines-initiative-launches-adapt-smart-an-adaptive-pathways-project-with-32-international-participants/

7.3.5. EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP)

Scope: PCWP plenary meeting held on 03 June 2015
Scope: PCWP/HCPWP joint meeting held on 04 June 2015
Scope: HCPWP meeting held on 04 June 2015

Action: for information

Documents:
Minutes

7.3.6. Questions and Answers on minimally manipulated ATMPs

CAT drafting group: M. Lipnik Stangelj (Rapp), P. Salmikangas (Rapp), T. Palomäki, E. Flory, M. Menezes Ferreira, P. Doevendans, M. Hrubiško
Scope: to create a Q&A document following the discussion that took place at the CAT-CHMP joint Strategic Review & Learning meeting in May 2015

Action: for information

7.4. Co-operation within the EU regulatory network

7.4.1. Analysis of European Clinical Trials Database (EudraCT)

CAT resources: M. Menezes-Ferreira, I. Reischl, T. Boráň, P. Salmikangas, N. Ferry, R. Mačiulaitis, D. Śladowski, M. Lipucci di Paola, B. Gänsbacher

Scope: Analysis of EudraCT for trials with ATMPs

Action: for discussion

7.4.2. Guideline on requirements for Investigational ATMPs

CAT drafting groups for investigational gene therapy and cell-based medicinal products: T. Palomäki (Rapporteur), I. Reischl (Rapp), M. Lipnik-Stangelj, M. Menezes Ferreira, M. O'Donovan, N. Ferry, S. Badoi, T. Boráň, C. Niederlaender

Action: for information

7.4.3. GMP requirements for ATMPs

Scope: European Commission consultation document has been released for external consultation: http://ec.europa.eu/health/files/advtherapies/2015_pc/publ_cons_doc_2015.pdf

Action: for information

Note: the draft GMP requirements for ATMPs (developed by CAT and the GMP inspectors) were published on the Commission website for external consultation until November 2015.

7.5. Co-operation with international regulators

7.5.1. International Pharmaceutical Regulators Forum (IPRF), New Orleans (USA), 13-16 May 2015

CAT resources: Nicolas Ferry

Scope: Feedback on IPRF Cell Therapy and Gene Therapy Groups

Scope: Feedback from the IPRF - Gene Therapy Working Group meeting

Action: for information

7.5.2. Health Canada: guideline on 'Cell Therapy Products in Clinical Trials'

Scope: guideline on quality, non-clinical and clinical requirement for applications for early and late clinical trials

Action: for information

7.5.3. Update on recent confidentiality arrangements with third country regulators and organisations

Action: for information

Note**:** CAT was informed that two confidentiality arrangements have been concluded by the European Commission DG SANTE and EMA in July and September 2015 respectively; the first with Swissmedic and the second with the WHO. Both arrangements are concluded for an initial period of 5 years, and may be renewed. Confidentiality agreements were already in place between EMA and the following international partners: USFDA, Japan PMDA/MHLW, Health Canada and TGA Australia.

Under the terms of confidentiality or working arrangements, the parties to the arrangement agree not to disclose non-public information, which means that product related information can be shared between the parties. The arrangements also facilitate ad hoc participation at product related discussions in response to specific requests.

7.6. CAT Work Plan

7.6.1. CAT Work Plan 2016

Scope: identification of projects and CAT topic leaders and participants for the different topics

CAT resources: Paula Salmikangas

Action: for discussion

7.6.2. CAT-ISCT Joint Workshop: 'Challenges and Opportunities for the Successful Development and Approval of Advanced Therapy Medicinal Products', Seville (Spain), Friday 25th September 2015, 14:15 – 18:45

CAT resources: Paula Salmikangas

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/06/news_detail_002357.jsp&mid=WC0b01ac058004d5c1

Action: for information

7.7. Planning and reporting

None

7.8. Others

7.8.1. International Society for Stem Cell Research (ISSCR): Guidelines for stem cell science and clinical transformation

Scope: review of ISSCR's Guidelines for stem cell science and clinical transformation

Action: for discussion

Note:
The draft guideline covers many fields starting from sourcing and manufacturing, non-clinical studies, ethical issues and clinical trials in early and late development, use in clinical care setting, access and economic question.

Comments received from the consulted committees and working parties/groups will be discussed during the September plenary meetings of the CAT and CHMP prior to forwarding them to ISSCR

7.8.2. Society for Immunotherapy on Cancer (SITC): chapters for a textbook on 'Cancer Immunotherapy'

Scope: contribution by CAT members to the textbook

Action: for discussion and appointment of co-authors

Note: the chapters will address quality, non-clinical and clinical aspects of cell therapy, gene therapy and combination cancer immunology products; the fourth chapter deals with companion diagnostics / immune monitoring: four to five co-authors from CAT are sought for each chapter. Deadline for completion of the manuscripts: April 2016.

CAT members interested to take part in the preparation of the four book chapter should inform the CAT secretariat by 16 September 2015.

7.8.3. Alliance for Regenerative Medicine: Stem Cell Conference 2015, 7-9 October, 2015, La Jolla, Mesa, CA, USA.

CAT resources: Ján Kyselovič

Scope: cell therapy, gene therapy and tissue engineering sectors together with the academic research community to advance scientific discovery and commercial development. Ján Kyselovič will attend.

Action: for information

Note: http://alliancerm.org/event/stem-cell-meeting-mesa

8. Any other business

Date of next CAT meeting:
Thursday 15th – Friday 16th October 2015

Explanatory notes

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

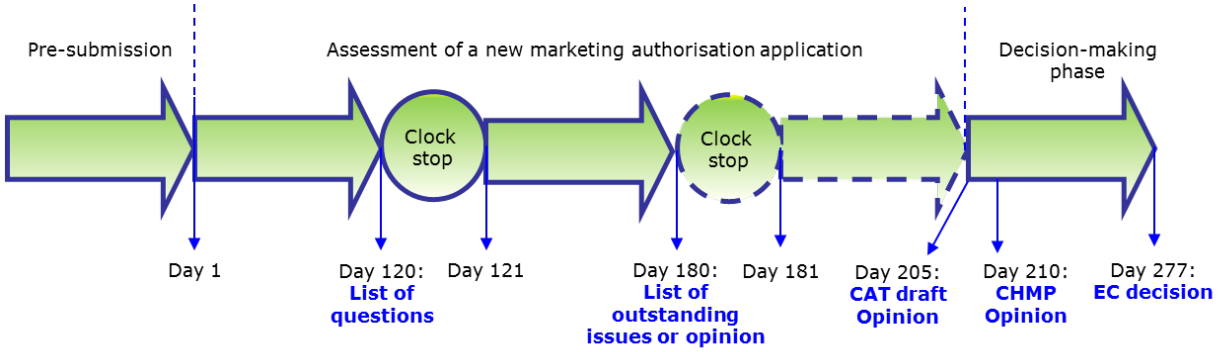
Evaluation of ATMPs (section 2)

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.

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/