EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13th March 2014
EMA/CAT/150740/2014 rev. 3
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda of the 13th – 14th March 2014 meeting

Chair: Paula Salmikangas, Vice-chair: Vacant

13th March 2014, 11:00hrs – 18:30hrs, Room 3A
14th March 2014, 09:00hrs – 13:00hrs, Room 3A

Election of CAT Vice-Chairperson. Call for nomination

Note: the nomination letter shall include a mission statement in support of the candidature

For information:
Procedure for the election of CAT Vice-Chair

For discussion:
Nominations received:

Declaration on conflict of interest

In accordance with the Agency's revised policy and procedure on the handling of conflicts of interests, participants in this meeting are asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests). Discussions, deliberations and voting will take place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee Secretariat at the start of meeting.

Health & 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 regards to therapeutic indications listed against products, it must be noted that these may not reflect the full wording proposed by the applicant and may also vary during the course of the review. The procedures discussed at CAT are on-going and therefore certain aspects are considered confidential. Additional details on some of the procedures (for example the ATMP classification procedure) will be published in the CAT monthly report. For orphan medicinal products the product name and the applicant are published to be consistent with already publicly available information. Of note, this agenda is a working document primarily designed for CAT members and the work the Committee undertakes. Further information with relevant explanatory notes can be found at the end of this document.

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Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present following a request for access to documents under 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).

1. PLENARY RELATED DOCUMENTS

1.1. AGENDA (EMA/CAT/58386/2014) and **TIMESCHEDULE** (EMA/CAT/58385/2014) for the CAT plenary to be held on 13th and 14th March 2014: **for adoption**

1.2. TABLE OF DECISIONS CAT plenary held on 13th and 14th January 2014 (EMA/CAT/792076/2013): **for information**

1.3. MINUTES of the CAT plenary held on 13th and 14th January 2014 (EMA/CAT/51170/2013): **for adoption**

1.4. 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 of 13th – 14th March 2014: **for information**

See March 2014 minutes (to be published post April 2014 CAT meeting)

2. EVALUATION OF ATMPS

2.1. OPINION
No items on the agenda

2.2. ORAL EXPLANATION
No items on the agenda

2.3. LIST OF QUESTIONS
No items on the agenda

2.4. DAY 80 ASSESSMENT REPORT
No items on the agenda

2.5. RE-EXAMINATION PROCEDURE (NEW APPLICATIONS)+UNDER ARTICLE 9(2) OF REGULATION No 726/2004
No items on the agenda

2.6. WITHDRAWAL OF APPLICATION
No items on the agenda

2.7. ONGOING EVALUATION PROCEDURES
No items on the agenda

2.8. NEW APPLICATIONS

2.8.1. (talimogene laherparepvec) (EMA/H/C/H0002771).
Therapeutic indication: treatment of adults with unresectable or metastatic melanoma.
For information:
- Nominations received for Rapporteurship:
- Nominations received for Co-rapporteurship:
- Nominations received for Peer reviewers:

2.8.2. Characterized viable haploidentical Herpes Simplex Virus Thymidine Kinase (HSV-Tk) and Human Low Affinity Nerve Growth Factor Receptor (ΔLNGFR) transfected donor lymphocytes) (EMEA/H/C/002801) Therapeutic indication: adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies.
For information:
- Review timetable

2.9. GMP and GCP INSPECTIONS REQUESTS

No items on the agenda

2.10. POST-AUTHORISATION

2.10.1. Type II Variations

2.10.1.1. Glybera (EMEA/H/C/002145) MAH: UniQure Biopharma B.V. *Orphan* **II/25** **Scope:** update of section 5.1. to allow for standard genetic testing to be used as an alternative to CE marking testing **For adoption:** ▪ Draft opinion	CAT Rapporteur: E. French (UK) CHMP Co-ordinator: G. Markey (UK)

2.10.2. Other PA Activities

2.10.2.1. ChondroCelect (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) (EMA/H/C/00878). MAH: TiGenix N.V. **Scope:** Five-year renewal **For adoption:** ▪ Draft opinion	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinator: J. Müller-Berghaus (DE)
2.10.2.2. ChondroCelect (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) MAH: TiGenix N.V. (EMA/H/C/00878/016) **Scope:** Randomised control trial protocol TIG/ACT/04/2009 **For adoption:** ▪ Draft AR on MAH's responses to the RSI	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinator: J. Müller-Berghaus (DE)
2.10.2.3. ChondroCelect (characterised viable autologous cartilage cells expanded *ex vivo* expressing specific marker proteins) MAH: TiGenix N.V. (EMA/H/C/00878/018) **Scope:** Non-interventional registry on the use of ChondroCelect to document the clinical effectiveness and safety outcome of treatment with ChondroCelect in real life in a patient population within the authorised indication **For adoption:** ▪ Draft AR on MAH's responses to the RSI	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinator: J. Müller-Berghaus (DE)

2.10.2.4.	**PROVENGE** (autologous peripheral blood mononuclear cells activated with pap-gm-csf (sipuleucel-T)). MAH: Dendreon UK Ltd. (EMA/H/C/002513) **Scope MEA 009:** re-evaluate the CD54 up-regulation acceptance criterion, based on quality and clinical data from patient batches manufactured in Europe, when sufficient data is available. **For adoption:** ▪ Rapporteur's AR circulated on 17.02.2014	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinators: J. Müller-Berghaus (DE)

3. CERTIFICATION

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

4. SCIENTIFIC RECOMMENDATION ON CLASSIFICATION OF ATMPs

4.1.	[Nuclear fraction separated from autologous bone marrow aspirate]. Proposed indication: stage I-III of osteoarthrosis and osteochondral lesion **For discussion:** ▪ Response to the second list of issues received 10th February 2014 **For adoption:** ▪ ATMP Classification report
4.2.	[allogeneic genetically engineered TCR-/CD52-/RQR8+/CD19 CAR+ T cells]. Proposed indication: CD19+ B-cell lymphomas **For adoption:** ▪ ATMP Classification report
4.3.	[characterised viable autologous stem cells expanded in vitro]. Proposed indication: treatment of degenerative arthritis, osteoarthritis (OA), articular cartilage defects in the knee, ankle or hip joints. **For adoption:** ▪ ATMP Classification report

4.4. [autologous collagen type II-specific regulatory Treg lymphocyte expanded population]. Proposed indication: treatment of inflammatory eyes diseases and inflammatory articular diseases **For information:** ▪ Request received on 21st February 2014 **For adoption:** ▪ Appointment of CAT Co-ordinator ▪ Timetable	
4.5. [polyethylene terephthalate (PET) scaffold seeded with autologous bone marrow derived mononuclear cell]. Proposed indication: reconstruction of trachea subsequent to damage or stenosis due to cancer, injury or infection. **For information:** ▪ Request received on 27th February 2014 **For adoption:** ▪ Appointment of CAT Co-ordinator ▪ Timetable	An ITF Briefing meeting took place in November 2013
4.6. Reflection paper on classification of ATMPs. **For discussion and adoption:** ▪ Revision of section 2.2.3.: 'reflections on homologous/non-homologous use'	Meeting scheduled for 13th March 18.30 - 19:30, room 3C

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.

6. PRE-AUTHORISATION ACTIVITIES

No items on the agenda

7. ITF BRIEFING MEETINGS IN THE FIELD 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.

8. ORGANISATIONAL MATTERS

8.1. Regulatory and Procedural Guidance

8.1.1. Article 57(p) of Regulation (EC) No. 726/2004 EC Scientific opinion request. Follow-up request from the European Commission – DG SANCO (B2 Unit) under Article 57(p) of Regulation (EC) No. 726/2004 **For discussion:**	EMA Co-ordinators: Previously discussed in January 2013
8.1.2. Legislation on tissues and cells: legislative proposals on importation of tissues and cells and on coding system for each donation: **for discussion**	

8.2. CAT Meeting Organisation

8.2.1. Election of Vice-Chairperson to CAT. Call for nomination **For discussion**: Nominations received:	*Note: the nomination letter shall include a mission statement in support of their candidacy*
8.2.2. CAT Membership **For information:** ▪ Latvia: Jānis Ancāns – stood down from his member role on 27th February 2014	
8.2.3. CAT/CHMP/COMP joint informal meeting to be held in Rome on 28th – 30th October 2014 under the auspices of the Italian Presidency of the Council of the European Union **For discussion:** ▪ Topics for agenda	
8.2.4. CAT/PDCO joint informal meeting hosted by the Heads of the Italian and Slovenian NCAs in November 2013 **For adoption:** ▪ Draft minutes	
8.2.5. CAT-MMD architecture: upgrade: **for information**	

8.3. Co-ordination with Committees/WPs/SAGs

8.3.1. Creation of the Inter-Committee Scientific Advisory Group (IC-SAG) for Oncology (which will replace the former SAG Oncology):
Call for nomination for core members:

Nominations to be sent to by 31.03.14.

*Note: core members **cannot** be members or alternates of any committee but rather external **clinical experts** to be proposed for nomination by committee members. They should be experts in the fields of clinical oncology, haematological oncology, paediatric oncology, or biostatistics. There is no limit to the number of nominations, the proposal will go to all the committees, to the Scientific Coordination Board and for final appointment by the CHMP*

8.3.2. CHMP February 2014 ToD: **for information**

8.3.3. COMP March 2014 agenda: **for information**

8.4. CAT's Work Programme

8.4.1. Objectives 2014-2015
For agreement on objectives for 2014:
- Oral feedback on a proposal for a joint CAT-DGTI workshop (11 September 2014)
  Appointment of Organising/programme committee members
- Discussion of scientific topics identified for horizon scanning
- Appointment of CAT member(s) to analyse and review of existing guidelines

9. CAT's DGs / PCWP and HCPWP

9.1. DG on GTMP Guidelines

9.2. DG on CTMP and TEP Guidelines

9.2.1. Reflection paper on clinical aspects related to TEPs
For adoption:
- Reflection paper
- List of Comments

9.2.2.	CAT workshop on Cell based therapies for Cardiac Repair scheduled for 14th-15th May 2014 **For information:** ▪ List of participants **For discussion:** ▪ Draft agenda **For nomination:** ▪ Proposed moderators for each section	

10.OTHER SCIENTIFIC TOPICS

10.1.	CAT international interactions – overview. **For action:** ▪ Call for candidatures for CAT members to take part in Regulators Forum Gene Therapy Discussion Group (RFGTDG) and Regulators Forum Cell Therapy Discussion Group (RFCTDG)	
10.2.	European Clinical Trials Framework. Regulation of the EP and the Council on clinical trials on medicinal products for human use and transparency initiatives **For information:** ▪ Presentation on the published document	The clinical trial Regulation was adopted by the EU in December 2013.
10.3.	DIA annual meeting in June 2014, San Diego, USA. Request for a CAT speaker to give a talk on the approval of regenerative medicines in the EU and support to developers by EMA/CAT **For information:** ▪ Dariusz Śladowski will represent the CAT in this meeting	
10.4.	Joint MHRA and BIA Innovation Conference on 19th June 2014 in Central London. Request for a CAT speaker to give a talk on ATMPs: scientific and regulatory considerations **For appointment of speaker from CAT**	Send your expression of interest to no later than 10 March 2014.
10.5.	Participation as CAT representative to scientific meetings and publications: **for discussion**	

11.A.O.B.

11.1. Multinational assessment teams: for discussion

11.2. Project 2014: move to 30, Churchill Place, Canary Wharf
For information:
- Update presentation

Date of next CAT meeting:
Tuesday 15th – Wednesday 16th April 2014

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CAT agenda and should be read in conjunction with the agenda or the minutes.

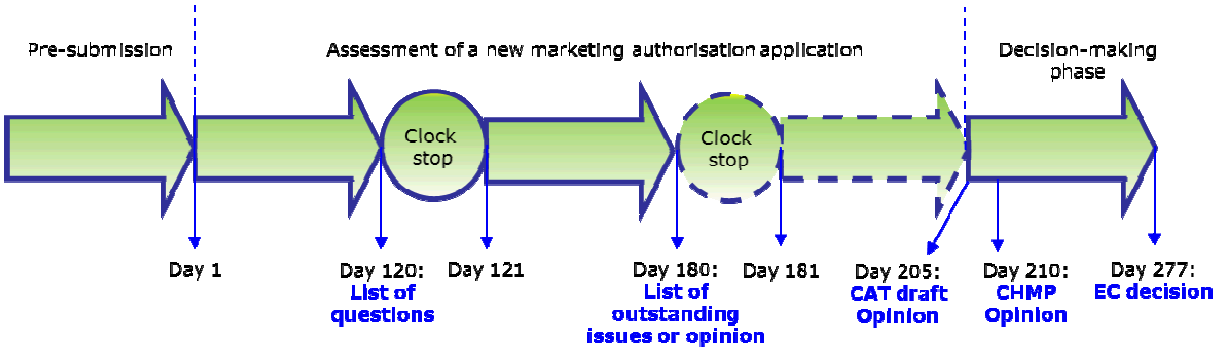
Evaluation of ATMPs (section 2)

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 2.9*)

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 2.3) 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 2.5*)

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 2.6*)

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 2.8*)

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.

Inspections Issues (*section 2.9*)

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 2.10*)

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.

ATMP Certification (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)

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 (Section 7)

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 matters (section 8)

This section includes topics related to Regulatory and Procedural Guidance, CAT meeting organisation (including CAT membership) and Co-ordination with other Committees, Working Parties, Scientific Advisory Groups and other groups.

CAT's DGs / PCWP and HCPWP (section 9)

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, the EMA/CAT-Notified Body Collaboration Group, the Patient and Consumer Working Party (PCWP) and the Healthcare Professionals Working Party (HCPWP).

Other Scientific Topics (section 10)

This section 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.