16 October 2014
EMA/CAT/541592/2014
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda of the 16 – 17 October 2014 meeting

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

16th October 2014, 10:00hrs – 18:30hrs, Meeting room 2-F
17th October 2014, 09:00hrs – 15:00hrs, Meeting room 2-F

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.

Note on access to documents

Some documents mentioned in the agenda/minutes cannot be released at present within the framework of Regulation (EC) No 1049/2001 on access to documents because 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. PLENARY RELATED DOCUMENTS

1.1. AGENDA (EMA/CAT/541592/2014) and **TIMESCHEDULE** (EMA/CAT/600212/2014 /2014) for the CAT plenary to be held on 16th and 17th October 2014: **for adoption**	
1.2. TABLE OF DECISIONS CAT plenary held on 18th and 19th September 2014 (EMA/CAT/577831/2014): **for information**	
1.3. MINUTES of the CAT plenary held on 18th and 19th September 2014 (EMA/CAT//2014): **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 16th – 17th October 2014: **for information**	*See October minutes (to be published post October 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 OUTSTANDING ISSUES

2.3.1. (formerly known as GPLSCD01) (*ex vivo* expanded autologous human corneal epithelial cells containing stem cells). (EMA/H/C/H0002450). Therapeutic indication: indicated for the treatment of patients with moderate-severe (superficial corneal neovascularisation in at least two quadrants) limbal stem cell deficiency, unilateral or bilateral with minimum 1-2 mm² of undamaged limbus, due to ocular burns. Strength: 790-3160 cells/mm^2. Pharmaceutical form: living tissue equivalent

For discussion:

- BWP report

For adoption:

- LoOIs

2.4. LIST OF QUESTIONS

No items on the agenda

2.5. DAY 80 ASSESSMENT REPORT

No items on the agenda

2.6. RE-EXAMINATION PROCEDURE (NEW APPLICATIONS)+UNDER ARTICLE 9(2) OF REGULATION No 726/2004

No items on the agenda

2.7. WITHDRAWAL OF APPLICATION

No items on the agenda

2.8. ONGOING EVALUATION PROCEDURES

2.8.1. (previously known as MM-TK) (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 discussion:

- Letters from the applicant dated 30th September 2014, requesting a clock-stop to respond to the D120 LoQs

For adoption:

- Timetable to response to LoQs

2.9. NEW APPLICATIONS

No items on the agenda

2.10. GMP and GCP INSPECTIONS REQUESTS

No items on the agenda

2.11. POST-AUTHORISATION

2.11.1. Type II Variations

No items on the agenda

2.11.2. Other PA Activities

2.11.2.1. Glybera (alipogene tiparvovec) (EMEA/H/C/2145) MAH: UniQure Biopharma B.V. *Orphan*

For discussion:

- Letter by the MAH dated 17.09.14. requesting a further extension of the clock-stop for specific obligation for introduction of virus removal step in manufacturing process (ANX004)

CAT Rapporteur: E. French
CHMP Coordinator: Greg Markey
PTL: C. Drai

Note: upon agreement by CAT, the company will submit a variation to amend the Annex II to the opinion.

2.11.2.2.	**PROVENGE** (autologous peripheral blood mononuclear cells activated with pap-gm-csf (sipuleucel-T)). MAH: Dendreon UK Ltd. (EMA/H/C/002513/ANX/001) **Scope:** to establish and keep an observational EU-based registry of men with mCRPC (Therapy in Men with Metastatic Castrate-Resistant Prostate Cancer) to evaluate overall survival, the risk of ischemic stroke or myocardial infarction following treatment with Provenge and other identified and potential risks (observational study P13-1) **For information:** ▪ PASS Protocol PRAC AR	CAT Rapporteur: E. Flory (DE) CHMP Co-ordinators: J. Müller-Berghaus (DE) EMA EPL: C. Vleminckx EMA PM: M. Nieto-Gutierrez *Adopted at PRAC in October 2014*

3. CERTIFICATION

Disclosure of information related to this section 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.	[lyophilised genetically modified Lactococcus (L. lactis) strin sAGX0354]. Proposed indication: intended for the reduction of the signs and symptoms, and induction and maintenance of clinical remission in patients with moderately active ulcerative colitis (UC). **For discussion:** ▪ Comments received by the Commission on 30 September 2014 **For adoption:** ▪ Revised ATMP Classification report

4.2. [platelet generated from in-vitro derived megakaryocytes]. Proposed indication: intended for the treatment of thrombocytopenia in patients at risk of bleeding or with haemorrhagic events

For discussion:

- Request from the applicant dated 26.09.14. to re-discuss the classification of non-ATMP

For adoption:

- Appointment of CAT Co-ordinator
- Timetable

4.3. [adeno-associated virus (AAV) vector carrying a gene for bacterial halorhodopsin]. Proposed indication: intended for the treatment of retinitis pigmentosa.

For adoption:

- ATMP Classification report

4.4. [allogeneic cord blood cells, *ex vivo* modulated with 16,16 dimethyl prostaglandin E2 (dmPGE2/ FT1050)]. Proposed indication: intended for the treatment of patients undergoing allogeneic hematopoietic reconstitution after high dose conditioning therapy for haematologic malignancies and certain rare genetic disorders.
Orphan

For adoption:

- ATMP Classification report

4.5. [human embryonic stem cell derived retinal pigment epithelial cells]. Proposed indication: intended for the treatment of age-related macular degeneration and Stargardt's macular dystrophy.

For adoption:

- ATMP Classification report

4.6. [autologous differentiated adipose cells isolated from adipose tissue]. Proposed indication: intended for the treatment of primary perianal fistula

For adoption:

- ATMP Classification report

4.7. [living human mesenchymal stem cells derived from Wharton's jelly tissue of umbilical cord].

Proposed indications:

1. Acute and chronic Graft-versus-Host-Disease (aGvHD and cGvHD);
2. Cartilage lessions;
3. Cerebral palsy;
4. Amyotrophic lateral sclerosis (ALS)

For adoption:

- ATMP Classification report

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

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 Plan (PIP)

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. Multinational Assessment Teams for initial marketing authorisation applications.

For discussion:

- Registry to list possible/available CAT-related expertise/resources in each MS for MN-teams

8.1.2. Application of ATMP Regulation

For information:

- Feedback from EMA to the Commission's letter of 1st July 2014 requesting mapping of requirements of cell and gene therapies for MAs: mapping exercise

For discussion:

- Aspects to consider. Presentation by L. Barkholt
- Oral feedback from the CAT reflection group on Risk Based Approach

CAT reflection groups:
- Quality related issues:
- Risk based approach:

8.1.3. Review of the initial MAA process. Update on the consultation workshop with NCAs that took place in early September 2014: **for information**

8.2. CAT Meeting Organisation

8.2.1. CAT Membership
For information:
Czech Republic:
- Tomáš Boráň – becomes member (from his former position of alternate) nominated on 1st October 2014
- Ivana Haunerova – becomes alternate (from her former position of member) nominated on 1st October 2014

8.2.2. 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 information:
- Agenda
- CAT final participation list

8.3. Co-ordination with Committees/WPs/SAGs

8.3.1. CHMP September 2014 ToD: **for information**

8.3.2. COMP October 2014 agenda: **for information**

8.4. CAT's Workplan

8.4.1. CAT Workplan 2015-2016: **for discussion**

Note: the draft workplan 2015-2016 developed on basis of discussion at the September 2014 CAT meeting. CAT is asked to discuss the draft programme and to appoint CAT topic leaders and other CAT participants for the 4 WP activities identified.

8.5. Interested Parties to CAT

8.5.1. CAT meeting with interested parties during the December CAT meeting **For discussion:** ▪ Agenda topics	*Tentative meeting dateThursday 11 December from 15.00 – 18.00. The CAT plenary meeting would run on 11 December from 10.00 to 15.00 and on Friday from 9.00-15.00. All timings are provisional.*

9. CAT's DGs / PCWP and HCPWP

9.1. DG on GTMP Guidelines

No items on the agenda

9.2. DG on CTMP and TEP Guidelines

No items on the agenda

9.3. PCWP and HCPWP

No items on the agenda

10.OTHER SCIENTIFIC TOPICS

10.1. Meeting between CAT and Competent Authorities for tissues and cells: **for discussion** **For information:** ▪ Minutes of the meeting between CAT and Competent Authorities for tissues and cells of 13 February 2012	Paula Salmikangas In September, CAT appointed two CAT members to attend a meeting with the Competent Authorities for tissues and cells (CA T&C) in December 2014.
10.2. Council of Europe – Guide to the Quality and Safety of Tissues and Cells for Human Application, second edition **For discussion:** ▪ Chapters 20, 21 and 23 related to ATMPs	Marta Lopez-Fraga – EDQM Iona Siska – EC-SANCO Esteve Trias-Adroher – CAT *Note: the Council of Europe is preparing a revision of the Tissues & Cells Guide. Chapters 20, 21 and 23 are making reference to ATMP and are significantly extending the scope of chapter 20 ATMP, 1st edition TC guide.*

10.3.	European Directorate for the Quality of Medicines & HealthCare (EDQM): General chapter 5.2.12 on raw materials used in the production of ATMPs **For information:** ▪ Publication in Pharmeuropa 26.4 (01 October 2014) of the general chapter 5.2.12 on raw materials used in the production of ATMPs. CAT comments can be sent to the following address: http://pharmeuropa.edqm.eu/home/.	Paula Salmikangas CAT members-EDQM WP members: P. Salmikangas, S. Ruiz, M. Menezes-Ferreira and L. Åkerblom, S. Saarela, L. Bisset and MT. Duffour Note: an EDQM/EMA meeting with ATMPs manufacturers and manufacturers of raw materials took place in April 2013. The EDQM WP have been working on the drafting of a general chapter of the raw materials using a *'family'* approach to define the quality requirements. The commenting period runs for 5 months from October (3 months public and 2 months for NPAs to collate responses). Information on how comments can be made on the EDQM website is provided in the following link: http://www.edqm.eu/site/how_to_commentpdf-en-31354-2.html
10.4.	The EMA's Executive Director – Guido Rasi's invitation to the CAT members to welcome the new building.	
10.5.	Veterinary medicines: setting up of a trilateral meeting with the Center of Veterinary Medicines of FDA (US) and Health Canada as a Stem Cell Working Group Trilateral meeting **For appointment:** ▪ CAT member to participate in the trilateral TC on 17th October from 14:00 – 16:00hrs (room 9C): S. Ruiz and M. Timón	The topics proposed by FDA for discussion include:

11.A.O.B.

11.1.	Quarterly report of planed MAAs with already appointed Rapporteurs: **for information**	
11.2.	11th Annual Phacilitates Cell & Gene Therapy Forum 2015, 26th-28th January 2015, Washington DC (USA) **For information:** ▪ M. Schüssler-Lenz will present the EU regulatory perspective (*tbc*)	

11.3. Inauguration Meeting and the Affiliated International Conference of Cellular Therapy organized by the Taiwan Association of Cell Therapy (TACT) on 5th December 2014 in Taipei (Taiwan)

For information:

- B. Sarkadi will present on the subject of cell therapy

Date of next CAT meeting:
Thursday 13th – Friday 14th November 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.

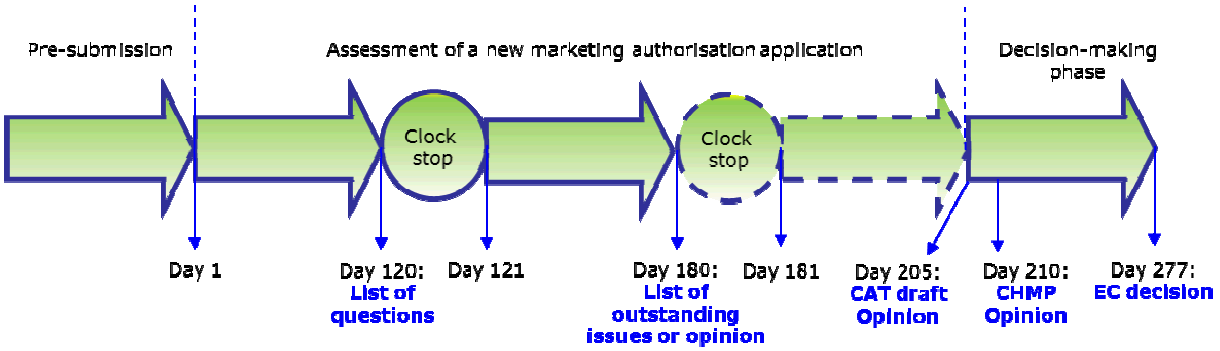
Evaluation of ATMPs (section 2)

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 2.6.*)

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.

Inspections Issues (*section 2.10.*)

This section lists inspections that are undertaken for ATMPs. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Post-authorisation activities (*section 2.11.*)

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.