EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 February 2014
EMA/CAT/95789/2014
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Minutes of the 16th – 17th January 2014 meeting

Chair: vacant, Vice-chair: Paula Salmikangas

DECLARATION OF CONFLICT OF INTEREST

In accordance with the Agency's revised Policy and Procedure on the handling of conflicts of interests, participants in this meeting were asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests). No additional conflicts of interest were declared.
Discussions, deliberations and voting took 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. The discussion, deliberations and voting took place in the presence of 22 CAT members (quorum reached).

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 cannot be released at present as they are currently in draft format or are classified as confidential. They will become public when adopted in their final form 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/737884/2013) and **TIMESCHEDULE** (EMA/CAT/13248/2014) for the CAT plenary to be held on 16th and 17th January 2014: **for adoption**	Adopted without amendments
1.2. TABLE OF DECISIONS CAT plenary held on 12th and 13th December 2013 (EMA/CAT/792076/2013): **for information**	Noted
1.3. MINUTES of the CAT plenary held on 12th and 13th December 2013 (EMA/CAT/ 800897/2013): **for adoption**	Adopted without amendments
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 January 2014: **for information**	See January 2014 minutes (to be published post February 2014 CAT meeting) No additional conflicts were declared

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. NEW APPLICATIONS

2.7.1. (allogeneic human heterologous liver cells) (EMA/H/C/003750). Therapeutic indication: treatment of urea cycle disorders. **For adoption:** ▪ Timetable	The review timetable was adopted.

2.8. PRE-SUBMISSION ISSUES

No items on the agenda

2.9. ONGOING EVALUATION PROCEDURES

No items on the agenda

2.10. PAEDIATRIC INVESTIGATION PLAN

No items on the agenda

2.11. GMP and GCP INSPECTIONS REQUESTS

No items on the agenda

2.12. VARIATIONS

2.12.1. Type II Variations

2.12.1.1. Glybera (EMEA/H/C/002145) MAH: UniQure Biopharma B.V. Orphan	CAT Rapporteur: Elaine French CHMP Co-ordinator: Greg Markey
II/05 (quality) **Scope:** **For discussion:** ▪ Letter from the applicant dated 16 January 2014 requesting an extension of clock stop **For adoption:** ▪ Revised response timetable	II/05: CAT agreed with the requested clock stop extension. The revised timetable was adopted.
II/29 (quality) **Scope:** **For adoption:** ▪ Opinion	II/29: CAT adopted by consensus the opinion for variation II/29
II/30 (clinical) **Scope:** Update of Protocol for the CM efficacy and safety study requested in the Annex II **For adoption:** ▪ Timetable	II/30: The proposal amendment to the Chylomicron study was already discussed and agreed by CAT in July 2013 (assessed as post-authorisation measure). This variation is to introduce the updated protocol in the Annex II. The review timetable for variation II/30 was adopted. This variation will be finalised together with the annual reassessment.

2.12.2. Other Post-Authorisation Activities

2.12.2.1. Glybera (alipogene tiparvovec) (EMEA/H/C/2145) MAH: UniQure Biopharma B.V. Orphan. Annual Reassessment **For adoption:** ▪ Draft opinion or RSI	CAT Rapporteur: Elaine French CHMP Co-ordinator: Greg Markey CAT adopted the Request for Supplementary information and the response timetable. The request for an updated RMP to be submitted was clarified.
2.12.2.2. PROVENGE (autologous peripheral blood mononuclear cells activated with pap-gm-csf) (EMA/H/C/2513). MAH: Dendreon UK Ltd. **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:** ▪ Timetable	CAT Rapporteur: Egbert Flory CHMP Co-ordinator: Jan Müller-Berghaus CAT adopted the evaluation timetable

3. CERTIFICATION

No items on the agenda

4. SCIENTIFIC RECOMMENDATION ON CLASSIFICATION OF ATMPs

4.1. [a suspension of allogeneic unrelated, buffy coat derived activated viable leukocytes]. Proposed indication: treatment of chronic lower extremity ulcers in adult diabetic patients **For adoption:** ▪ Revised ATMP Classification report	*Comments received from the European Commission* CAT adopted by consensus the revised ATMP classification report. This product is classified as a somatic cell therapy product.
4.2. [Cultured autologous skin substitute using acellular human donor dermis as matrix]. Proposed indication: wound healing **For information:** ▪ ATMP Classification report	The European Commission raised no comments. This product is classified as a tissue engineered product.
4.3. [a cell suspension of autologous skeletal myoblast]. Proposed indication: oculo-pharyngeal muscular dystrophy **For information:** ▪ ATMP Classification report	*The European Commission raised no comments.* *This product is classified as a tissue engineered product.*

4.4.	[Nuclear fraction separated from autologous bone marrow aspirate]. Proposed indication: stage I-III of osteoarthrosis and osteochondral lesion **For discussion:** Response to the list of issues **For adoption:** Revised ATMP Classification report	CAT discussed the responses provided by the applicant. Additional information from the applicant is required before CAT can finalise this classification request. This information relates to the claim of the company that the use of this products in osteochondral lesions should be considered 'homologous' and the claimed mechanism of action. A second list of issues was adopted via written procedure until 23 January evening and thereafter transmitted to the applicant.
4.5.	[autologous *ex vivo* expanded leukocytes treated with 5-aza-2'-deoxycytidine]. Proposed indication: solid tumours. **For adoption:** ▪ ATMP Classification report	The CAT adopted by consensus the draft scientific recommendations prepared by the CAT Rapporteur. CAT secretariat to send the draft scientific recommendation to the Commission for comments until 30 January 2014 The CAT recommendation will be considered final if no comments are received from the Commission. The final report will be sent thereafter to the Applicant.

5. SCIENTIFIC ADVICE

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

6. ORPHAN DRUG DESIGNATION

6.1.	Committee for Orphan Medicinal Products (COMP) **For information:** ▪ Agenda for the meeting 7th–8th January 2014	COMP Secretariat The information was noted.

7. OTHER TASKS OF THE CAT

7.1. ITF Briefing Meetings in the field of ATMPs

No items on the agenda

7.2. Other ITF Briefing Meetings of interest to CAT

No items on the agenda

7.3. International Co-operation

No items on the agenda

8. ELIGIBILITY AS ATMP AND RAPPORTEURSHIP

No items on the agenda

9. ORGANISATIONAL MATTERS

9.1. Regulatory and Procedural Guidance

9.2. CAT Meeting Organisation

9.2.1. CAT/PDCO joint informal meeting hosted by the Heads of the Italian and Slovenian agencies, held on 25th-26th November 2013 **For information:**	Postponed until the February CAT meeting
9.2.2. Election of Chairperson to CAT. Call for nomination **For information**: ▪ Timelines	*Note: the nomination letter shall include a mission statement in support of the candidature* **Timetable:** -Call for election with supporting documents to be sent out by CAT Secretariat: mid-Jan. 2014 -Deadline for receipt of candidatures: 12.02.14. -Election: first agenda item at the CAT February meeting: 13.02.14. The information was noted.
9.2.3. CAT Membership **For information:** ▪ UK: Elaine French – new member nominated on 3rd January 2014	The information was noted.
9.2.4. Principles for publication of agendas and minutes of EMA scientific committees: **for information**	This document was adopted by the EMA management board in December 2013 and was circulated to CAT for information.

9.3. Co-ordination with Committees/WPs/SAGs/other groups

9.3.1. CHMP December 2013 ToD: for information

9.4. CAT interaction with Interested Parties

9.5. CAT Work Programme

9.5.1. Satellite CAT scientific workshop in the margins of the World Conference on Regenerative Medicine held in Leipzig (Germany) on 23-25 October 2013 **For information:** ▪ Feedback on the workshop	Postponed

10. CAT DGs/OTHER GROUPS

10.1. GTMP Guidelines

10.2. Guidelines for CTMP and TEP

10.2.1. Reflection paper on clinical aspects related to TEPs: **for discussion**	The Rapporteur presented the Reflection paper and informed the CAT of the comments received during the external consultation. CAT members to send written comments to the CAT secretariat by 7 February 2014. Adoption scheduled at the February CAT meeting.

10.3. EMA/CAT-NB Collaboration Group

10.4. PCWP guidelines

10.5. Healthcare Professionals WP

11. OTHER SCIENTIFIC GUIDELINES/ISSUES

11.1. 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:** ▪ Published agreed text	The clinical trial Regulation was adopted on 20 December 2013. A more detailed presentation will be made at the March CAT meeting.

12. PHARMACOVIGILANCE

13. A.O.B.

- CAT secretariat informed the Committee that an amendment will be made to the CAT Rules of Procedure to clarify how to calculate the quorum and majority. The revised Rules of Procedure will be included in the February CAT agenda for adoption.
- CAT Workshop on cell-based therapies for Cardiac Repair: CAT was informed on the status of the invitations of the experts.

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.

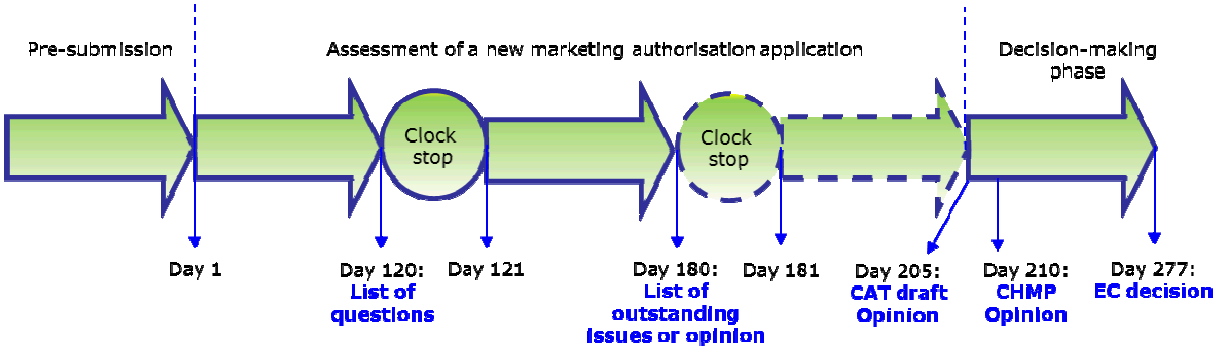
Evaluation of ATMPs (section 2)

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 the Paediatric Investigation Plans for ATMPs discussed by the Committee (*section 2.10*), any ATMP related inspection requests (*section 2.11*) and Post-authorisation activities (*section 2.12*)

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 2.9 (**Ongoing evaluation procedures**). Section 2.9 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 2.7*)

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.

Pre-submission (*section 2.8*)

In some cases the CAT may discuss an ATMPs 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.

Paediatric investigation Plans (*section 2.10*)

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.

Inspections Issues (*section 2.11*)

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.

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.

Orphan Drug Designation (section 6)

This section refers to the report from the Committee for Orphan Medicinal Products (COMP).

Other Tasks of the CAT (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 9)

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 Drafting groups / Other Groups (section 10)

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 Guidelines/issues (section 11)

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.

Pharmacovigilance (section 12)

Any non-product related Pharmacovigilance issue coming from the discussion of the PRAC will be listed here. PRAC issues related to ATMPs are included in section 2.12.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

List of participants: *including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 16-17 January 2014 meeting.*

CAT Member	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/ substance
Ilona Reischl	Austria	Full involvement	
Claire Beuneu	Belgium	Full involvement	
Sandra Tomljenovic	Croatia	Full involvement	
Ivana Haunerova	Czech Republic	Full involvement	
Sinan B. Sarac	Denmark	Full involvement	
Paula Salmikangas	Finland	Full involvement	
Nicolas Ferry	France	Full involvement	
Egbert Flory	Germany	Full involvement	
Zsuzsanna Buzás	Hungary	Full involvement	
Maura O'Donovan	Ireland	Full involvement	
Paolo Gasparini	Italy	Full involvement	
Jānis Ancāns	Latvia	Full involvement	
Hans Ovelgönne	Netherlands	Full involvement	
Marit Hystad	Norway	Full involvement	
Dariusz Śladowski	Poland	Cannot act as rapporteur ; Involvement in discussions only	ATMP classification
Mikuláš Hrubiško	Slovakia	Full involvement	
Metoda Lipnik-Stangelj	Slovenia	Full involvement	
Lennart Åkerblom	Sweden	Full involvement	
Pieter Doevendans	ESCARDIO	Full involvement	

CAT Alternate	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/ substance
Belaïd Sekkali	Belgium	Full involvement	
Ivica Malnar	Croatia	Cannot act as rapporteur ; Involvement in discussions only	Scientific Advice
Tomáš Boráň	Czech Republic	Full involvement	
Tarmo Tiido	Estonia	Full involvement	
Olli Tenhunen	Finland	Full involvement	
Sophie Lucas	France	Full involvement	
Martina Schüssler-Lenz	Germany	Full involvement	
Meave Lally	Ireland	Full involvement	
Guy Berchem	Luxembourg	Cannot act as rapporteur ; Involvement in discussions only	Post-authorisation activities
Anthony Samuel	Malta	Full involvement	
Rune Kjeken	Norway	Full involvement	
Margarida Menezes-Ferreira	Portugal	Full involvement	
Ján Kyselovič	Slovakia	Full involvement	
Marcos Timón	Spain	Full involvement	
Björn Carlsson	Sweden	Full involvement	
Mariette Driessens	EGAN	Cannot act as rapporteur/coordinator/peer reviewer	Scientific Advice
Esteve Trias-Adroher	EATB	Full involvement	
Ramadan Jashari	EATB	Full involvement	

EUROPEAN COMMISSION	Country	Outcome restriction following evaluation of e-DoI for the meeting	Topics on the current Committee Agenda for which restriction applies Product/ substance
Rocío Salvador-Roldán	European Commission	Full involvement	

*CAT Expert**	*Country*	*Outcome restriction following evaluation of e-DoI for the meeting*	*Topics on the current Committee Agenda for which restriction applies* *Product/ substance*
* Experts were only evaluated against the product they have been invited to talk about.			
Guido Panté	Italy	Full involvement	
Louise Bisset	United Kingdom	Full involvement	
Lisbeth Barkholt	Sweden	Full involvement	