EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 February 2015
EMA/CAT/81435/2015
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 19–20 February 2015

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

19 February 2015, 11:00hrs – 18:30hrs, room 2-F
20 February 2015, 09:00hrs – 15:00hrs, room 2-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 monthly reports once the procedures are finalised and start of referrals will also be available.

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

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts.

PRE-MEETING LIST of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session to be held 19-20 February 2015.	See February 2015 minutes (to be published post March 2015 CAT meeting)

1.2. Adoption of agenda of the meeting of 19-20 February 2015

1.3. Adoption of the minutes of the previous CAT meeting on 15-16 January 2015

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

No items on the agenda

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 Application)+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

No items on the agenda

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

2.11.1.1.	**Glybera** MAH: UniQure Biopharma B.V. (EMEA/H/C/002145/II/34) *Orphan* **II/34** **Scope:** submission of final study report AMT011-02 **For information:** **For adoption:** ▪ Revised timetable	CAT Rapporteur: E. French CHMP Co-ordinator: G. Markey See also 2.11.2.1.

2.11.2. Other PA Activities

2.11.2.1.	**Glybera** (EMEA/H/C/002145/S/0039), (alipogene tiparvovec), MAH: UniQure Biopharma B.V. *Orphan*. Second Annual Reassessment **For information:** ▪ Updated Rapporteur's assessment report **For adoption:** ▪ Draft Opinion	CAT Rapporteur: E. French CHMP Co-ordinator: G. Markey PRAC Rapporteur: J. Williams See also 2.11.1.1.
2.11.2.2.	**ChondroCelect** (characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins) MAH: TiGenix N.V. (EMA/H/C/00878/MEA 16.3 and 18.3) **Scope:** Randomised control trial protocol TIG/ACT/04/2009 **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 information:** **For adoption:** ▪ Revised timetable	CAT Rapporteur: E. Flory CAT Co-Rapporteur: T. Palomäki CHMP Co-ordinator: J. Müller-Berghaus **Revised timetable:**

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.

4. Scientific Recommendation on Classification of ATMPs

4.1. [adipose-derived mesenchymal stem cells]. Proposed indication: intended for the treatment of autoimmune diseases. **For information**: ▪ ATMP Classification report	*The European Commission raised no comments*
4.2. [tumour-infiltrating lymphocytes derived from metastatic melanoma]. Proposed indication: intended for the treatment of metastatic melanoma **For information**: ▪ ATMP Classification report	*The European Commission raised no comments*
4.3. [human extracellular matrix on a absorbable polymer matrix]. Proposed indication: intended for the surgical/ interventional treatment of congenital heart malformations **For discussion:** ▪ Comments received from the Commission dated 6th February 2015 **For adoption**: ▪ Revised ATMP Classification report	
4.4. [adult human bone-marrow derived, *ex-vivo* expanded, pooled allogeneic mesenchymal stromal cells]. Proposed indication: intended for thromboangiitis obliterans (Buerger's disease) **For adoption:** ▪ ATMP Classification report	
4.5. [autologous mononuclear cells derived from human cord blood]. Proposed indication: intended for paediatric brain damage, hypoxic-ischaemic encephalopathy, and cerebral palsy **For information:** ▪ Request received on 06.02.15. **For adoption:** ▪ Appointment of CAT Co-ordinator ▪ Timetable	
4.6. [suspension of allogeneic human adult stern cells, isolated from skeletal muscle]. Proposed indication: intended for the treatment of Duchenne Muscular Dystrophy (DMD) **For information:** ▪ Request received on 04.02.15. **For adoption:** **Appointment of CAT Co-ordinator** ▪ Timetable	

4.7.	[allogeneic *ex-vivo* expanded placental adherent stromal cells] Proposed indication: intended for Peripheral Arterial Occlusive Disease (PAOD). **For information:** ▪ Request received on 04.02.15. **For adoption:** **Appointment of CAT Co-ordinator** ▪ Timetable	
4.8.	[allogeneic somatic cells therapy medicinal product derived from the isolation and *ex vivo* expansion of human Umbilical Tissue-Derived Cells]. Proposed indication: improvement of visual acuity in patients with vision loss from geographic atrophy secondary to age-related macular degeneration. **For information:** ▪ Request received on 04.02.15. **For adoption:** **Appointment of CAT Co-ordinator** ▪ Timetable	
4.9.	[autologous dendritic cells loaded with autologous irradiated tumour stem cells suspended in a cryopreservation medium]. . Proposed indication: intended for the treatment of melanoma. **For information:** ▪ Request received on 02.02.15. **For adoption:** **Appointment of CAT Co-ordinator** ▪ Timetable	
4.10.	Reflection Paper on Classification of ATMPs **For discussion:** ▪ Update on the activities of the Drafting groups	Following CAT members will take part in the review of the comments received: - Drafting group on substantial manipulation: - Drafting group on non-homologous use

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)

6.1.1.	The PDCO requests the CAT's view on the acceptable levels of DMSO for children (to be consistent with future procedures) and whether they could provide recommendations on the maximum acceptable DMSO levels for the paediatric population: **for discussion**	– Paediatric Medicines Dept.

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.	Application of ATMP Regulation **For discussion:** ▪ Report from the joint telecon of the CAT reflection groups on quality-related issues and risk based approach ▪ Next steps	CAT reflection groups: - Quality related issues: - Risk based approach:
8.1.2.	Development of GMP requirements for investigational ATMPs **For discussion** ▪ Outcome of the DG meeting of 18.02.15.	CAT drafting group members:
8.1.3.	Joint SAWP/CAT/CHMP manuscript: *'Challenges related to development of Advanced Therapy Medicinal Products – an EMA/CAT/SAWP survey from past marketing authorization and scientific processes'* **For information:** ▪ Update of members of the Drafting Group and Reference Group	
8.1.4.	Benefit-risk project. New template for assessment reports: **for information**	

8.2. CAT Meeting Organisation

8.2.1.	CAT-CHMP joint Strategic Review & Learning meeting to be held in Ljubljana (Slovenia) on 26th-28th May 2015 under the auspices of the Latvian Presidency of the Council of the European Union **For information:** ▪ Practical information **For discussion:** ▪ Topics for the agenda	Note: the formerly known *'informal'* meetings have been renamed to *'Strategic Review & Learning'* meeting. This new name accurately illustrates the true purpose of such meetings as a key part of the work of the Committees.
8.2.2.	CAT/CHMP/COMP joint meeting that took place in Rome in October 2014 under the auspices of the Italian Presidency of the Council of the European Union **For information:** ▪ Minutes of the joint session **For discussion/adoption:** ▪ Minutes of the CAT break-out session	The minutes of the joint session have been adopted by CHMP and COMP.

8.2.3.	MMD. Training session to take place at the CAT March meeting. Send any questions/query/issues in advanced to CATSecretariat@ema.europa.eu: **for information**	
8.2.4.	Cross-Committee Task Force on Patient Registries. CAT members are requested to volunteer to join this task force **For information:** ▪ Description of the project and composition of this task force	Interested CAT members should inform the CAT secretariat by Friday 6th March 2015 See also 8.3.2.
8.2.5.	CAT Membership: Hungary: switch of roles of member and alternate: Krisztian Fodor becomes the member and Balázs Sarkadi becomes the alternate as of 19th February 2015	

8.3. Co-ordination with Committees/WPs/SAGs

8.3.1.	CHMP January 2015 ToD: **for information**	
8.3.2.	Oral feedback from the Scientific Co-ordination Board (SciCoBo) meeting of 29th January 2015 **For information:** ▪ Minutes of meeting 13.10.14. ▪ Report of meeting on 29.01.15.	See also 8.2.4. and 8.4.2.
8.3.3.	Question from Safety Working Party to CAT: non-clinical tumourigenicity studies for ATMPs: **for discussion**	Initial discussion on the ways to involve the SWP and the CAT in a common discussion around this subject.

8.4. CAT's Workplan

8.4.1. Joint CAT/ISCT workshop/satellite meeting to take place in the margins of the European Meeting of the ISCT to be held on 25 September 2015, Seville (Spain): '*What should and can we do to make cellular therapies that bring value to patients available to these patients as soon as possible?'* **For information:** ▪ Feedback from the first Programme Committee teleconference **For discussion:** ▪ Topics for the agenda ▪ E-mail from ISCT dated 13th February 2015 proposing topics for the CAT/ISCT workshop	This relates to Topic 4 in the CAT Workplan 2015-2016: *'Provide assistance to ATMP developers via the organisation of a scientific workshop in collaboration with a scientific society'*. Programme Committee members: A teleconference of the Programme Committee took place on 21st January 2015
8.4.2. CAT workplan 2015-2016: **for adoption**	See also 8.3.2. Further to presentation and discussion at the Scientific Coordination Board meeting of 29 January 2015, the CAT is asked to adopt their workplan 2015-2016

8.5. Interested Parties to CAT

No items on the agenda

9. CAT's DGs / PCWP and HCPWP

9.1. DG on GTMP Guidelines

9.1.1. Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products **For adoption:** ▪ Guideline for external consultation	

9.2. DG on CTMP and TEP Guidelines

9.2.1. Guideline on investigational ATMPs in clinical trails **For information:** ▪ Letter from European Commission dated 26th January 2015 **For appointment:** ▪ Drafting group members	- Drafting group members will be appointed at the February CAT meeting. CAT members interested to join this drafting group should inform the CAT secretariat. - A teleconference call will be organised in advance of the March CAT meeting to initiate the work of the drafting group.

9.3. PCWP and HCPWP

9.3.1.	Nomination of CAT members to join the HCPWP. **For information:** ▪ Job description	Olli Tenhunen stepped down in January 2015 Interested CAT members should inform the CAT secretariat by Friday 6th March 2015
9.3.2.	Draft Agenda EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting 4 March 2015: **for information**	
9.3.3.	Draft Agenda EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting: information session on Biosimilars 5 March 2015: **for information**	
9.3.4.	Minutes of the EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) meeting with all eligible organisations held in November 2014: **for information**	

10. Other Scientific Topics

10.1.	EMA/CAT/FDA/Health Canada bimonthly teleconference on ATMP cluster. **For information:** ▪ Minutes of the November 2014 TC **For adoption:** ▪ Agenda	Thursday 19th February 2015 18:30hrs – 19:30hrs, room 02-C
10.2.	Council of Europe – Guide to the Quality and Safety of Tissues and Cells for Human Application, second edition **For information:** ▪ Letter from EDQM to CAT chair dated 11th December 2014 ▪ Draft Guide, published for external consultation ▪ Communication from CAT chair to EDQM (dated 30 January 2015)	CAT provided comments on 18 November 2014 to EDQM/Council of Europe. The external consultation on the guideline expired on 31.01.15.
10.3.	Draft INN naming scheme for cell therapy products **For agreement:** ▪ Letter from EMA to WHO (including feedback from CAT and BWP) **For information**: ▪ INN scheme ▪ Comments by CAT and BWP	Note: the draft has been developed by the WHO INN secretariat in collaboration with the INN expert group.

10.4.	European Union Clinical Trial Regulation. Public consultation on application of transparency rules. Stakeholders to submit their comments by 18th February 2015: **for information**	The clinical trial regulation was adopted on 20 December 2013. An advanced e-mail informing of the public consultation deadline was sent out to CAT members on 29.01.15 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/01/news_detail_002253.jsp&mid=WC0b01ac058004d5c1
10.5.	Projects in Horizon 2020 related to ATMPs: current and future calls: **for information**	
10.6.	International Pharmaceutical Regulators Forum (IPRF) – Gene Therapy Working Group. In-person meeting in the margins of the ASGCT Annual Meeting (New Orleans, Louisiana, U.S.A., 13-16 May 2015). **For agreement:**	
10.7.	Joint meeting between CAT and Competent Authorities for tissues and cells / medicines **For information:** ▪ Joint meeting to take place on 23rd April 2015 (*tbc*) ▪ Letter from the CAT Chair dated 23rd January 2015 to DG Santé, Tissue and Cells Unit	
10.8.	Invitation to write scientific/regulatory articles for four scientific publications: **For discussion and agreement:** Requests from: 1. *Current Gene Therapy* (September 2014) 2. *BioMed Research International* (January 2015) for the special issue on MSC-based mesenchymal Regenerative Medicines 3. *Cell and Gene Therapy Insights* (February 2015 4. *Current Tissue Engineering* (February 2015)	*Current Gene Therapy*. In September 2014, following CAT members agree to contribute to the writing of an article:
10.9.	Similarity of orphan ATMPs **For discussion:** ▪ Question on the consequence of the Holoclar approval for their ATMP development ▪ E-mails on similarity of two GTMPs	

11. Any Other Business

No items on the agenda

Date of next CAT meeting:
Thursday 19th – Friday 20th March 2015

Explanatory notes

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

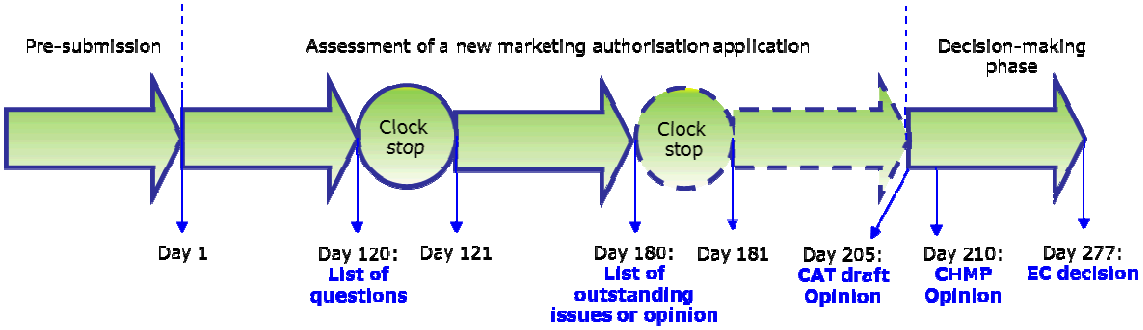
Evaluation of ATMPs (section 2)

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 2.9*)

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.

More detailed information on the adobe terms can be found on the EMA website: www.ema.europa.eu/