EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 November 2014
EMA/CAT/706533/2014
Procedure Management and Business Support Division

Committee for Advanced Therapies (CAT)

Agenda for the meeting on 13–14 November 2014

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

13 November 2014, 09:00hrs – 13:00hrs
14 November 2014, 09:00hrs – 13:00hrs

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.

MMD Connection Advice

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 13 - 14 November 2014.	See November 2014 minutes (to be published post December 2014 CAT meeting)
1.2. Adoption of agenda of the meeting of 13-14 November 2014	
1.3. Adoption of the minutes of the previous CAT meeting on 18-19 October 2014	
1.4. Table of Decisions of the previous CAT meeting on 18-19 October	

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** (alipogene tiparvovec) (EMEA/H/C/2145) MAH: UniQure Biopharma B.V. *Orphan* **II/37-G** **Scope:** Update of sections 4.8 and 5.1 of the SmPC **For adoption:** ▪ Request for Supplementary Information ▪ Timetable	CAT Rapporteur: E. French CHMP Coordinator: G. Markey
2.11.1.2.	**Glybera** (alipogene tiparvovec) (EMEA/H/C/2145) MAH: UniQure Biopharma B.V. *Orphan* **II/38** **Scope:** Update of section 5.1 of the SPC based on the final clinical study report **For adoption:** ▪ Request for Supplementary Information ▪ Timetable	CAT Rapporteur: E. French CHMP Coordinator: G. Markey

2.11.2. Other PA Activities

2.11.2.1.	**Glybera** (alipogene tiparvovec) (EMEA/H/C/2145/Anx 004) MAH: UniQure Biopharma B.V. *Orphan* **For discussion:** ▪ Letter from 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) ▪ Letter from the MAH dated 04.11.14. in response to the CAT's question on nanofiltration	CAT Rapporteur: E. French CHMP Coordinator: G. Markey Note: upon agreement by CAT, the company will submit a variation to amend the Annex II to the opinion. CAT to decide on the extended timeline for the introduction of the nanofiltration, after receipt of clarification from the MAH
2.11.2.2.	**Glybera** (alipogene tiparvovec) (EMEA/H/C/2145/PSUV/36) MAH: UniQure Biopharma B.V. *Orphan* **Scope:** PSUR **For information:** ▪ PRAC PSUR AR	CAT Rapporteur: E. French CHMP Coordinator: G. Markey *PSUR adopted at PRAC in November 2014* *PRAC Recommendation: maintenance*

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. [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 adoption**: ▪ ATMP Classification report	
4.2. [adeno-associated virus (AAV) vector carrying a gene for bacterial halorhodopsin]. Proposed indication: intended for the treatment of retinitis pigmentosa. **For information:** ▪ ATMP Classification report	See also 7.2. *The European Commission raised no comments*
4.3. [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 discussion:** ▪ Response to the LoQ received on 29th October 2014 **For adoption:** ▪ Revised ATMP Classification report	
4.4. [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 information:** ▪ ATMP Classification report	See also 5.4. *The European Commission raised no comments*
4.5. [autologous differentiated adipose cells isolated from adipose tissue]. Proposed indication: intended for the treatment of primary perianal fistula ▪ **For discussion:** ▪ Response to the LoQ received on 4th November 2014 **For adoption:** ▪ Revised ATMP Classification report	

4.6. [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 discussion** ▪ Comments raised by the Commission on 29th October 2014 **For adoption:** ▪ Revised ATMP Classification report	*Comments raised by the European Commission on two of the four therapeutic indications:* -acute and chronic GvHD; -cerebral palsy
4.7. [solid flexible implant with chondrocytes fixed in biodegradable human origin fibrin based excipient]. Proposed indication: intended for the treatment of focal non-arthrotic cartilage defects of Outerbridge Grade III or IV of the femoral condyle including the trochlea **For discussion:** ▪ Request for ATMP Classification received on 30.10.14. **For adoption**: ▪ Appointment of CAT Co-ordinator ▪ Timetable	See also 5.6.
4.8. Reflection Paper on Classification of ATMPs: overview of comments received during external consultation: **for discussion**	Appointment of drafting group(s) to review the comments

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 information:** ▪ Updated registry to list possible/available CAT-related expertise/resources in each MS for MN-teams	No additional comments received to the list of CAT-related expertise/resources in the MS of Multinational assessment teams.
8.1.2.	Application of ATMP Regulation **For discussion:** ▪ Oral feedback from the joint telecon of the CAT reflection groups on quality related issues and risk based approach ▪ 'Aspects to consider' on questions to SAWP of ATMPs'	CAT reflection groups: - Quality related issues: - Risk based approach: **Timetable** for document *'Aspects to consider on questions to SAWP on ATMPs'*: -Comments by CAT: Friday 5th December 2014 -Discussion at CAT: 11-12 December 2014
8.1.3.	Changes to the MAA process **For information** ▪ Presentation	
8.1.4.	Draft Guidance on meetings with applicants on responses to questions received from EMA Scientific Committees during the evaluation within the centralised procedure **For information:** ▪ draft guidance document	Committees drafting group members: **Timetable:** Comment by committees: 05.12.14 to

8.2. CAT Meeting Organisation

8.2.1.	CAT/CHMP/COMP joint informal meeting took place in Rome on 28th – 30th October 2014 under the auspices of the Italian Presidency of the Council of the European Union **For information:** ▪ Oral debriefing	
8.2.2.	CAT Membership **For information:** Cyprus: ▪ Maria Vasiliou terminated her alternate membership on 24.10.14. ▪ Ioannis Kkolos – new alternate member nominated on 25.10.14.	
8.2.3.	CAT Dates for 2015: **for information**	Patrick Celis External website: CAT meeting dates

8.3. Co-ordination with Committees/WPs/SAGs

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

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

8.4. CAT's Workplan

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

8.5. Interested Parties to CAT

8.5.1. CAT meeting with Interested Parties during the December CAT meeting
For discussion:
- Agenda topics

This meeting will take place on Thursday 11th December from 15.00 – 18.00 (the CAT plenary meeting will run on 11th December from 09.00 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

9.1.1. Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products: **for information**

9.2. DG on CTMP and TEP Guidelines

No items on the agenda

9.3. PCWP and HCPWP

9.3.1. Draft Work plan for the European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP): **for endorsement**

9.3.2. Draft Work plan for the European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP): **for endorsement**

10. Other Scientific Topics

10.1. Council of Europe – Guide to the Quality and Safety of Tissues and Cells for Human Application, second edition **For discussion:** ▪ Comments on Chapters 1, 20, 21 and 22 related to ATMPs	*Note: the Council of Europe is preparing a revision of the Tissues & Cells Guide. Chapters 1, 20, 21 and 22 are making reference to ATMP and are significantly extending the scope of chapter 20 ATMP, 1st edition TC guide.* CAT members to produce comments by 14th November 2014
10.2. Draft INN naming scheme for cell therapy products: **for discussion**	Note: the draft has been developed by the WHO INN secretariat in collaboration with the INN expert group.
10.3. EMA/CAT/FDA/Health Canada bimonthly teleconference on ATMP cluster **For information:** ▪ Minutes of the September 2014 ATMP cluster teleconference **For adoption:** ▪ Agenda	
10.4. '*Development pathways for advanced therapy medicinal products*': workshop organised by Emerging Biopharmaceutical Enterprises (EBE) in collaboration with EMA and Italian Embassy's Scientific Office in London – 15 December 2014 **For information:** ▪ Programme	CAT members interested to attend this workshop should inform the CAT Secretariat by 28 November 2014. Registration and agenda
10.5. Joint meeting between CAT and Competent Authorities for tissues and cells to take place in Brussels in the 1Q of 2015, to discuss topics of common interest. **For discussion:** ▪ Brainstorming for topics	Note that a similar meeting was held in February 2012.

11. Any Other Business

Date of next CAT meeting:
Thursday 11th – Friday 12th December 2014

Explanatory notes

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

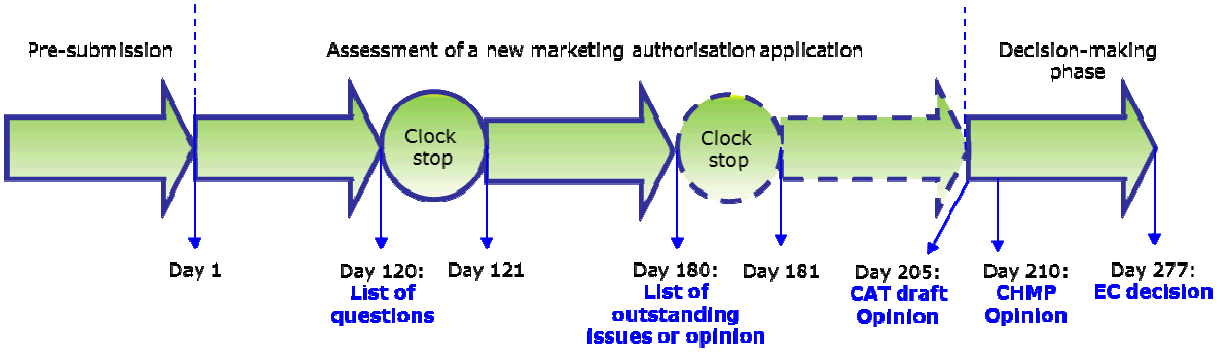
Evaluation of ATMPs (section 2)

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/