



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

20 April 2016  
EMA/CAT/310689/2016  
Procedure Management and Committees Support Division

## Committee for Advanced Therapies (CAT) Minutes of the meeting on 22-23 March 2016

Chair: Paula Salmikangas - Vice-chair: Martina Schübler-Lenz

22 March 2016, 09:00 – 18:30, room 02-A

23 March 2016, 09:15 – 17:00, room 02-A

### 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 the minutes 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 meeting reports once the procedures are finalised.

Of note, the minutes are a working document primarily designed for CAT members and the work the Committee undertakes.

### Note on access to documents

Some documents mentioned in the minutes 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 ongoing 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. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

### 1.2. Adoption of agenda

The CAT agenda for 22-23 March 2016 was adopted

### 1.3. Adoption of the minutes

The CAT minutes of 18-19 February 2016 were adopted with amendments to sections 3.2.1 and 4.2.6.

## 2. Evaluation of ATMPs

### 2.1. Opinions

#### 2.1.1. Strimvelis – Autologous CD34+ cells transduced with retroviral vector containing the adenosine deaminase gene; *Orphan*; EMA/H/C/003854

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GlaxoSmithKline Trading Services - UK; treatment of children aged 0-18 diagnosed with adenosine deaminase deficiency and for whom no suitable human leukocyte antigen-identical sibling bone marrow donor is available

Scope: Opinion

**Action:** for adoption

Documents:  
Draft CAT AR  
Draft Opinion  
BWP report

Notes:  
LoQs adopted: 18.09.2015  
Accelerated assessment granted: 17.04.2015

The Rapporteurs presented the outcome of the assessment of list of questions.

CAT reviewed the obligation linked to the approval and the quality and clinical commitments.  
CAT proposed a rewording of the first clinical commitment .  
CAT discussed the summary of product characteristics and the labelling.  
CAT adopted by consensus the positive CAT draft opinion and CAT assessment report. CHMP adopted the opinion at its March 2016.

## 2.2. Oral explanations

No items

## 2.3. Day 180 List of outstanding issues

### 2.3.1. Characterised viable haploidentical herpes simplex virus thymidine kinase (HSV-Tk) and human low affinity nerve growth factor receptor ( $\Delta$ LNGFR) transfected donor lymphocytes; *Orphan*; EMA/H/C/002801

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MolMed SpA; Treatment of adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies

**Action:** for adoption

Document:  
-LoOIs  
-BWP report

Revised Timetable:

List of Outstanding Issues adopted on 20.03.2015. List of Questions adopted on 18.07.2014.

The CAT Rapporteurs presented the outcome of the assessment of the responses to the list of outstanding issues.

The outcome of the PRAC discussion on the RMP was presented.

CAT adopted by consensus the third list of outstanding issues, which included the issues to be addressed in the oral explanation.

## 2.4. Day 120 Lists of questions

No items

## 2.5. Day 80 assessment reports

No items

## 2.6. Ongoing initial full application

No items

## 2.7. New applications

## 2.8. Withdrawal of initial marketing authorisation application

No items

## 2.9. Re-examination of initial application procedures under Article 9(2) of Regulation no. 726/2004

No items

## 2.10. GMP and GCP inspections requests

No items

## 2.11. Type II variations

No items

## 2.12. Other post-authorisation activities

### 2.12.1. ChondroCelect – Characterised viable autologous cartilage cells expanded *in vivo* expressing specific marker proteins; EMA/H/C/00878/MEA 020

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TiGenix N.V.

Rapporteur: Egbert Flory; CHMP Coordinators: Jan Müller-Berghaus

Scope: MEA 020 Interim report/Study TGX001-2011. Area: clinical

**Action:** for adoption

Documents:

Draft Assessment Report

CAT agreed with the outcome of the assessment by the Rapporteur.

## 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.

### 3.1. Opinions

No items

### 3.2. Day 60 evaluation reports

No items

### 3.3. Ongoing initial application

No items

### 3.4. New applications

No items

## 4. Scientific Recommendation on Classification of ATMPs

### 4.1. New requests – appointment of CAT Co-ordinators

#### 4.1.1. Allogeneic bone marrow derived mesenchymal cells (MSC) expanded *ex vivo* in synthetic media

---

Intended for the treatment of acute graft-versus-host disease grades III and IV resistant to first line treatment

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.2. Concentrate of autologous bone marrow-derived mononuclear cells (BM-MNC)

---

Intended for the improvement of heart function (left ventricular ejection fraction) and quality of life in patients with ischaemic post-acute myocardial infarction and in chronic heart disease

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 9<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.3. Live-attenuated, double-deleted *Listeria monocytogenes* (Lm) expressing human mesothelin

---

Intended for the treatment of non-small cell lung cancer

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 7<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.4. Live-attenuated, double-deleted *Listeria monocytogenes* (Lm) expressing prostate antigens

---

Intended for the treatment of prostate cancer



Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 7<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.5. Autologous cultured fibroblasts

---

Intended for the indications of:

- Facial skin regeneration;
- Reducing facial wrinkles;
- Treatment of deep lines in the skin;
- Tissue loss and to heal chronic non-closing injuries;
- Treatment of acne scars

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 10<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.6. Extracellular matrix from adipose tissue

---

Intended for the treatment of non-healing wounds

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.7. Adipose derived mesenchymal cells (MSC)

---

Intended for the treatment of non-healing wounds

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.8. Bone marrow derived mesenchymal cells (MSC)

---

Intended for the treatment of children's encephalopathy, children's epilepsy, children's spinal cord injury

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:  
Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.9. Autologous cultured chondrocytes

---

Intended for the treatment of filling of cartilage loss in knee-joint

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:  
Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.10. Autologous cultured fibroblasts

---

Intended for the treatment of filling of skin connective tissue loss

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:  
Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure

#### 4.1.11. Autologous cultured keratinocytes

---

Intended for the treatment of non-healing wounds, burns, trophic ulcers

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:  
Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.12. Autologous cultured myoblasts

---

Intended for the treatment of faecal and urinary incontinence and of skeletal muscle injury

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:  
Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

#### 4.1.13. Autologous cultured melanocytes

---

Intended for the treatment of vitiligo

Scope: appointment of CAT Co-ordinator and adoption of timetable

**Action:** for adoption

Document:

Request received 12<sup>th</sup> March 2016

Nominations were received. The CAT member was appointed as the CAT coordinator for this procedure.

## 4.2. Day 30 Co-ordinators' first reports

### 4.2.1. Autologous *ex vivo* expanded polyclonal CD4<sup>+</sup>CD25<sup>+</sup>CD127<sup>lo/-</sup>FOXP3<sup>+</sup> regulatory T cells

---

Intended for the treatment of type 1 diabetes mellitus

**Action:** for adoption

Document:

ATMP classification report

CAT discussed the ATMP classification report. CAT adopted by consensus the ATMP classification reports. CAT secretariat to send the draft scientific recommendation to the European Commission for comments

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

### 4.2.2. DNA plasmid encoding a recombinant fusion protein consisting of the extracellular domain of human tumour necrosis factor *alpha* p55 receptor linked to the human immunoglobulin G1 Fc domain

---

Intended for the treatment of refractory chronic non-infectious uveitis

**Action:** for adoption

Document:

ATMP classification report

CAT discussed the ATMP classification report. CAT adopted by consensus the ATMP classification reports. CAT secretariat to send the draft scientific recommendation to the European Commission for comments.

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

### 4.2.3. Autologous stromal vascular fraction

---

Intended as an autologous lipofiller

**Action:** for adoption

Document:

ATMP classification report

CAT discussed the ATMP classification report. CAT considered that the claim: intended as an autologous lipofiller is not a therapeutic indication; the company is advised to contact the relevant national authority for the classification of their product for the use as autologous lipofiller.

#### 4.2.4. Autologous human bone marrow mononuclear cells

---

Intended for the treatment type 2 diabetes mellitus

**Action:** for adoption

Document:  
ATMP classification report

CAT discussed the ATMP classification report. CAT adopted by consensus the ATMP classification reports. CAT secretariat to send the draft scientific recommendation to the European Commission for comments

The CAT recommendation will be considered final if no comments are received from the European Commission. The final report will be sent thereafter to the applicant.

### 4.3. Day 60 Co-ordinators' revised reports following List of Questions

#### 4.3.1. Autologous adipose-derived regenerative cells encapsulated in carboxymethylcellulose

---

Intended for autologous dermal filling

**Action:** for adoption

Document:  
ATMP classification report  
Applicant responses to LoQs

Note: CAT adopted in January 2016 a two-month clock stop to allow the applicant time to respond to the LoQs.

CAT discussed the updated ATMP classification report (updated following receipt of the additional information from the applicant). In line with the discussion on autologous stromal vascular fraction (see 4.2.3) the report will be revised. CAT considered that the claim: intended for autologous dermal filling is not a therapeutic indication; the company is advised to contact the relevant national authority for the classification of their product for autologous dermal filling.

### 4.4. Finalisation of procedures

#### 4.4.1. Human burn eschar and debrided adipose tissue cells

---

Intended for the treatment of burns and non-healing wounds

Different product formulations:  
-hBEDATCs in suspension  
-hBEDATCs as sheet  
-hBEDATCs on acellular amniotic matrix  
-hBEDATCs on acellular dermal matrix

**Action:** for adoption

Document:  
Revised ATMP classification report  
Comments from the European Commission dated 3<sup>rd</sup> March 2016

The revised report was adopted.

#### 4.4.2. Co-culture of keratinocytes and human burn eschar and debrided adipose tissue cells

---

Intended for the treatment of burns and non-healing wounds

Different product formulations:

-hBEDATCs on acellular amniotic matrix

-hBEDATCs on acellular dermal matrix

**Action:** for information

Document:

ATMP classification report

Note: The European Commission raised no comments

The information was noted.

#### 4.4.3. Recombinant non-replicative serotype 5 human adenovirus containing sequences coding for the core protein, polymerase protein and selected domains of the envelope protein of hepatitis B virus (Genotype D)

---

Intended for the treatment of chronic hepatitis B

**Action:** for information

Document:

ATMP classification report

Note: The European Commission raised no comments

The information was noted.

#### 4.4.4. Irradiated, whole-cell, allogeneic tumour immunotherapy

---

Intended for the treatment of pancreatic cancer

**Action:** for information

Document:

ATMP classification report

Note: The European Commission raised no comments

The information was noted.

#### 4.4.5. Autologous Epstein-Barr virus specific T-cells derived from peripheral blood mononuclear cells, expanded *ex vivo*

---

Intended for the treatment of Epstein-Barr Virus (EBV) positive malignancies

**Action:** for information

Document:

ATMP classification report

Note: The European Commission raised no comments

The information was noted.

#### 4.4.6. Hematopoietic stem and progenitor cells (HSPC) genetically modified with zinc finger nucleases (ZFNs) to disrupt the erythroid enhancer (ENH) of the gene encoding the human transcription factor BCL11A

---

Intended for the treatment of  $\beta$ -thalassemia

**Action:** for adoption

Documents:

Revised ATMP classification report

Comments from the European Commission dated 3<sup>rd</sup> March 2016

Further to the comments from the European Commission, CAT discussed further the justification of the classification outcome. CAT was not able to conclude on this report as additional information from the company was needed. CAT adopted a LoQs.

#### 4.4.7. Autologous cells of stromal vascular fraction (SVF) and autologous adipose derived stem cells

---

Intended for treatment of keloid scars and aging skin

**Action:** for adoption

Documents:

Revised ATMP classification report

Comments from the European Commission dated 3<sup>rd</sup> March 2016

The revised report was adopted.

### 4.5. Follow-ups and guidance

No items

## 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.

### 5.1. New requests – appointment of CAT Co-ordinators

### 5.2. CAT Rapporteurs' reports

### 5.3. Lists of issues

### 5.4. Finalisation of Scientific Advice procedures

## 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 plans (PIP)

## 6.2. ITF briefing meetings in the field of ATMPs

# 7. Organisational, regulatory and methodological matters

## 7.1. Mandate and organisation of the CAT

### 7.1.1. Strategic Review & Learning meeting

---

CAT-PDCO-CTFG joint Strategic Review & Learning meeting will take place in Utrecht, Netherlands on 1<sup>st</sup>-2<sup>nd</sup> June 2016 under the auspices of the Dutch Presidency of the Council of the European Union

CAT resources: Hans Ovelgönne

Scope: initial discussion to agree on topics for the agenda. The scientific focus will be on dose finding in the context of extrapolation to children

**Action:** for discussion

Document:  
Draft agenda

Note: CAT members are asked to send proposals for agenda topics

H Ovelgönne presented the draft agenda. On the first day, sessions with PDCO and with CTFG are scheduled. On the second day, there is a CAT only session: CAT members to provide suggestions to the CAT secretariat.

### 7.1.2. Changes to the participation of alternate members in the meetings of the scientific committees (when there is no appointment member)

---

**Action:** for information

Document:  
Principles for invitation to alternates to committees meetings.

It is now clarified that the alternate member can be invited and reimbursed and will be able to vote when the position of the corresponding member becomes vacant (e.g. after resignation).

### 7.1.3. New internal guidance on management of confidentiality and declarations of interests for observers participating in EMA scientific meetings

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**Action:** for information

Note:

The Agency has developed internal guidance on observers participating in EMA scientific meetings, focusing on management of confidentiality and declarations of interests.

Observers from a non-EEA authority or organisation with no Confidentiality Arrangement in place with EMA require a personal Confidentiality undertaking only (no Declaration of Interests (DoI) /Curriculum vitae (CV)).

The following do not require a personal Confidentiality undertaking (no DoI/CV): Observers from European Institutions and European Union; Observers from non-EEA authorities or organisations with a Confidentiality Arrangement (CA) in place with EMA.

EEA National Competent Authorities (NCAs) staff members are considered as European experts: a DoI including a Confidentiality Undertaking and CV is required. *Exception: non-scientific administrative staff from NCAs attending EMA meetings on a one off / ad hoc basis: a personal CU is required, but no DoI/CV.*

The information was noted.

#### 7.1.4. New CAT plenaries dates and times – from April 2016

---

Scope: agreement by the EMA's Executive Director to the change in meeting times (from current timing of Thurs 09.00 – Fri 15.00 to new timing of Weds 14.00 - Fri 12.00, to accommodate CAT workload and needs)

**Action:** for information

Note: The CAT discussed and agreed on the new times at its plenary in February 2016. The main drivers for this change were: need for additional time for discussion, updating and adoption of milestone documents (e.g. draft opinion on MAA); increase in workload (especially on pre-submission procedures and for guideline / CAT work topic development). It was clarified that the duration of the meeting will depend on the topics on the agenda (CAT meeting could finish earlier or could even take place virtually). Within the new timing, ITF meetings could be organised either on Wednesdays before 14.00 or Fridays after 12.00.

The new timing was noted. The April meeting will start on Wednesday 20<sup>th</sup> April and finish on Thursday 21<sup>st</sup> April.

## 7.2. Coordination with EMA Scientific Committees

### 7.2.1. Committee for Medicinal Products for Human Use (CHMP)

---

Scope: Summary of Outcomes (SoO) for the February 2016 meeting

**Action:** for information

Documents:  
-Summary of Outcomes

The information was noted.

### 7.2.2. Early access tools: initial marketing authorisation - revised accelerated assessment (AA) guideline

---

Scope: amended guideline and timetables

**Action:** for information

Note: the CHMP adopted the new guideline at its February 2016 plenary meeting

A presentation was given on the revised accelerated assessment (AA) guideline and the procedural timetables.

### 7.2.3. Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

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Scope: CHMP guideline on conditional marketing authorisation

**Action:** for information



Note: the CHMP adopted the guideline at its February 2016 plenary meeting.

A presentation was given on the revised guideline on conditional approvals.

### 7.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

#### 7.3.1. CAT – CHMP (SWP) cluster on tumourigenicity studies for ATMPs

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CAT resources: Tiina Palomäki, Hans Ovelgönne, Björn Carlsson, Egbert Flory; Carla Herberts and Isabelle Vieira; Scope: update on progress regarding drafting of the reflection paper and discussion on how to best progress the topic

**Action:** for discussion

Documents:

-CAT-SWP cluster – Minutes of the 2<sup>nd</sup> teleconference that took place on 28<sup>th</sup> October 2015  
-Draft proposal for reflection paper on non-clinical tumourigenicity studies for cell-based medicinal products

CAT agreed to provide an extract from the analysis of EudraCT (ongoing) on trials with ATMPs (including name of the product, EudraCT number). This information will be used by the drafting group members to look at precedents regarding what Quality/NC data was used to approve the trial (with focus on data defining tumourigenic potential of the product).

### 7.4. Co-operation within the EU regulatory network

#### 7.4.1. Orphan similarity for ATMPs

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CAT drafting group: Margarida Menezes-Ferreira, Nicolas Ferry, Paula Salmikangas, Ilona Reischl, Christiane Niederlaender, Michele Lipucci;

Scope: Reflection from the perspective of ATMPs on the concept of 'similar active substance' as referred to in Art 3(3)c of Reg (EC) No 847/2000 of April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concept 'similar medicinal product' and 'clinical superiority'

Scope: feedback from the breakout meeting of 23<sup>rd</sup> March 2016

**Action:** for discussion

The final proposal addressing similarity for ATMPs, prepared by the CAT drafting group members, was presented. A minor change was proposed by CAT. The revised CAT proposal on similarity for ATMPs was adopted. The comment from the drafting group to extend the ATMP similarity proposal to biologicals for which the principal molecular structural features (PMSF) cannot be defined was noted: this will have to be discussed and agreed with BWP/CHMP.

EMA will incorporate the CAT proposal with the proposals prepared by QWP (for chemicals) and BWP (for biologicals). The consolidated proposal will be sent to the European Commission.

#### Post-meeting note.

During its March meeting, CHMP adopted the proposal for PMSF for chemicals and biologicals (prepared by QWP and BWP). The comment from the CAT drafting group to extend the ATMP proposal to biologicals for which the PMSF cannot be defined was not implemented. The consolidated proposal has been sent to the European Commission.

## 7.5. Co-operation with international regulators

### 7.5.1. ATMP cluster teleconference with FDA / Health Canada / PMDA

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The teleconference will take place during the plenary meeting on Tuesday 22<sup>nd</sup> March from 14.00hrs – 15.00hrs

CAT resources: Paula Salmikangas

**Action:** for information

Document table:  
Draft agenda

The agenda was agreed.

### 7.5.2. International Pharmaceutical Regulators Forum (IPRF) Gene therapy group (7 January and 9 March 2016)

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CAT resource: Paula Salmikangas

Scope: oral feedback from the teleconference that took place on 7<sup>th</sup> January and 9<sup>th</sup> March 2016

**Action:** for information

Documents:  
Agenda

Topic postponed to the April CAT meeting.

## 7.6. CAT Work Plan

### 7.6.1. CAT workshop for cell-based cancer immunotherapy products (15-16 November 2016)

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CAT resources: Rune Kjekken, Björn Carlsson, Olli Tenhunen, Martina Schübler-Lenz, Metoda Lipnik-Stangelj, Paula Salmikangas, Marit Hystad, Dariusz Sladowski, Bernd Gänsbacher

Scope: feedback from teleconference of 11<sup>th</sup> March 2016

**Action:** for information

Feedback was provided by the organising/programme Committee. The workshop will address regulatory and scientific aspects for cell-based cancer immunotherapies; quality, non-clinical and clinical sessions will be planned. The organising/programme Committee will continue to develop the agenda and proposals for speakers.

### 7.6.2. CAT assessor training (23-24 June 2016)

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Moderators: for Quality session: Margarida Menezes-Ferreira and Ilona Reischl; Clinical session: Martina Schübler-Lenz and Simona Badoi; Non-clinical session: Björn Carlsson and Egbert Flory

**Action:** for information

Note: a breakout meeting took place on Monday 21<sup>st</sup> March 2016

A short feedback was given on the progress of the organisation of this training. Some CAT members will be approached soon to ask if they could give presentations / case studies at the CAT assessors training. EMA will reimburse one representative (assessor) per member state,

but the assessor training will also be available via the EU-Network Training Centre allowing colleagues in the member states to join remotely (Adobe Connect).

### 7.6.3. Guideline on requirements for investigational ATMPs

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CAT drafting groups: Tiina Palomäki (Rapporteur), Ilona Reischl (Rapp), Metoda Lipnik-Stangelj, Margarida Menezes Ferreira, Maura O'Donovan, Nicolas Ferry, Simona Badoi, Tomas Boráň, Christiane Niederlaender

Scope: Feedback from the drafting group meeting of 22<sup>nd</sup> March 2016

**Action:** for information

An outline of the structure of the above guideline was provided. CAT will be kept informed of the progress.

## 7.7. Planning and reporting

No items

## 7.8. Others

### 7.8.1. International Society for Cellular Therapy (ISCT) 2016 Annual Meeting, Singapore, 25-28 May 2016

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Scope: request by ISCT for a CAT expert. Martina Schübler-Lenz to speak on the quality and operations track session: *'Evolving regulatory regime for cell based therapies – faster/early access'*

**Action:** for adoption on participation

Note: the session will focus on regulatory pathways such as adaptive licensing or conditional licensing; Japan: Reg Med Law; EU: adaptive licensing pilot or PRIME; and US FDA: breakthrough, are proposed to talk.

Programme: [http://www.isct2016.com/wp-content/uploads/2016/03/ISCT-2016-Preliminary-Program\\_WEB.pdf](http://www.isct2016.com/wp-content/uploads/2016/03/ISCT-2016-Preliminary-Program_WEB.pdf)

CAT agreed with the participation of Martina Schübler-Lenz as CAT representative to the ISCT annual meeting.

## 8. Any other business

### 8.1.1. EMA notification system

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Scope: Test of the EMA emergency notification system – RapidReach

**Action:** for information

EMA informed the CAT members of the EMA emergency notification system and what to do in case they receive a RapidReach call/text message.

Date of next CAT meeting:  
Wednesday 20<sup>th</sup> to Thursday 21<sup>st</sup> April 2016

## 9. Explanatory notes

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

### Abbreviations / Acronyms

AR: Assessment Report

ATMP: Advanced Therapy Medicinal Product

BWP: Biologics Working Party

CAT: Committee for Advanced Therapies

CHMP: Committee for Medicinal Product for Human Use

COMP: Committee for Orphan Medicinal Products

DG: Drafting Group

EC: European Commission

FL: Final Letter

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Environmental Risk Assessment

GMP: Good Manufacturing Practice

HTA: Health Technology Assessment Bodies

HSPC: Hematopoietic Stem and Progenitor Cells

ITF: Innovative Task Force

JR: Joint Report

LoOI: List of outstanding issues

LoQ: List of questions

MA: Marketing Authorisation

MAA: Marketing Authorisation Applicant

MAH: Marketing Authorisation Holder

MSC: Mesenchymal stem cells

PDCO: Paediatric Committee

PMDA: Pharmaceuticals and Medical Devices Agency (Japan)

PIP: Paediatric Investigation Plan

PL: Package leaflet

PRAC: Pharmacovigilance and Risk Assessment Committee #

PRIME: Priority Medicines

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SA: Scientific Advice

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party  
SR: Summary Report  
SWP: Scientific Working Party  
SME: Small and medium size enterprises  
SmPC: Summary of Products Characteristics  
TT: Timetable

## 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 2.12.)*

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.

### *GMP and GCP 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 2.12.)*

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.

## **Certification of ATMPs (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)**

### *Paediatric Investigation Plan (PIP)*

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*

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, regulatory and methodological matters (section 7)**

This section includes topics related to regulatory and procedural guidance, CAT workplan, CAT meeting organisation (including CAT membership), planning and reporting, co-ordination with other committees, working parties and scientific advisory groups.

Furthermore, 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, cooperation within the EU regulatory network and international regulators as well as direct interaction with interested parties. It also 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.

## **Any other business (section 8)**

This section is populated with miscellaneous topics not suitable under the previous headings.

More detailed information on the above terms can be found on the EMA website: [www.ema.europa.eu/](http://www.ema.europa.eu/)

## List of participants

including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 22-23 March 2016 meeting.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Paula Salmikangas	Chair	Finland	No interests declared	
Iлона Reischl	Member	Austria	No interests declared	
Claire Beuneu	Member	Belgium	No interests declared	
Belaid Sekkali	Alternate	Belgium	No interests declared	
Evelina Shumkova	Alternate	Bulgaria	No interests declared	
Ivica Malnar	Alternate	Croatia	No interests declared	
Tomáš Boráň	Member	Czech Republic	No interests declared	
Ivana Haunerova	Alternate – by TC	Czech Republic	No interests declared	
Nanna Aaby Kruse	Member	Denmark	No restrictions applicable to this meeting	
Toivo Maimets	Member	Estonia	No interests declared	
Tiina Palomäki	Member	Finland	No interests declared	
Nicolas Ferry	Member	France	No interests declared	
Violaine Closson	Alternate	France	No interests declared	
Martina Schüssler-Lenz	Member (Vice-Chair)	Germany	No interests declared	
Asterios Tsiftoglou	Member	Greece	No interests declared	
Krisztian Fodor	Member	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No restrictions applicable to this meeting	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Johannes Hendrikus Ovelgönne	Member	Netherlands	No interests declared	
Marit Hystad	Member	Norway	No interests declared	
Rune Kjekken	Alternate	Norway	No restrictions applicable to this	



Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			meeting	
Dariusz Śladowski	Member	Poland	No restrictions applicable to this meeting	
Margarida Menezes-Ferreira	Alternate (to CHMP representative)	Portugal	No interests declared	
Simona Badoi	Member	Romania	No interests declared	
Mikuláš Hrubíško	Member	Slovakia	No restrictions applicable to this meeting	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Björn Carlsson	Alternate	Sweden	No interests declared	
Christiane Niederlaender	Member	United Kingdom	No interests declared	
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Mariëtte Driessens	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Sotirelis Chris	Expert - in person*	Italy	No interests declared	
Guido Panté	Expert - in person*	Italy	No interests declared	
Paula van Hennik	Expert - via telephone*	Netherlands	No interests declared	
Sabine Straus	Expert - via telephone*	Netherlands	No interests declared	
Brigitte Keller-Stanislowski	Expert - via telephone*	Germany	No interests declared	
Riaz Zuhrie	Expert - via telephone*	UK	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

\* Experts were only evaluated against the agenda topics or activities they participated in.