



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

15 October 2015  
EMA/CAT/723417/2015  
Procedure Management and Committees Support Division

## Committee for Advanced Therapies (CAT)

### Minutes of the meeting on 17-18 September 2015

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

17 September 2015, 09:00 – 18:30, room 02-F

18 September 2015, 09:00 – 15:00, room 02-F

#### Disclaimers

Some of the information contained in this set of 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 and start of referrals will also be available.

Of note, this set of minutes 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 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 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).



## Table of contents

<b>1.</b>	<b>Introduction</b>	<b>5</b>
1.1.	Welcome and declarations of interest of members, alternates and experts .....	5
1.2.	Adoption of agenda.....	5
1.3.	Adoption of the minutes of the July 2005 meeting .....	5
1.4.	August Written Procedure .....	5
<b>2.</b>	<b>Evaluation of Advanced Therapy Medicinal Products</b>	<b>5</b>
2.1.	Opinions .....	5
2.2.	Oral explanations .....	6
2.2.1.	Talimogene laherparepvec; EMA/H/C/0002771 .....	6
2.3.	D180 List of outstanding issues (LoOIs) .....	6
2.4.	D120 Lists of questions (LoQs) .....	6
2.4.1.	Autologous CD34+ cells transduced with retroviral vector containing the adenosine deaminase gene; <i>Orphan</i> ; EMA/H/C/003854 .....	6
2.5.	Day 80 assessment reports.....	6
2.6.	Re-examination procedure (new applications) under Article 9(2) of Regulation No. 726/2004 .....	6
2.6.1.	Heparesc - Allogeneic human heterologous liver cells; <i>Orphan</i> ; EMA/H/C/003750 .....	6
2.7.	Withdrawal of initial full application .....	7
2.8.	Ongoing initial full application .....	7
2.9.	New applications .....	7
2.9.1.	Expanded adipose-derived stem cells of allogeneic origin; <i>Orphan</i> ; EMA/H/C/0004258 .....	7
2.10.	GMP and GCP inspections requests .....	7
2.11.	Type II variations .....	7
2.11.1.	Glybera – Alipogene tiparvovec; <i>Orphan</i> ; EMA/H/C/002145/II/34 .....	7
2.11.2.	Glybera – Alipogene tiparvovec; <i>Orphan</i> ; EMA/H/C/002145/II/37-G .....	8
2.11.3.	Glybera – Alipogene tiparvovec; <i>Orphan</i> ; EMA/H/C/002145/II/38 .....	8
2.11.4.	Glybera – Alipogene tiparvovec; <i>Orphan</i> ; EMA/H/C/002145/II/46-G .....	8
2.12.	Other post-authorisation activities .....	9
2.12.1.	Holoclar – <i>Ex vivo</i> expanded autologous human corneal epithelial cells containing stem cells; <i>Orphan</i> ; EMA/H/C/002450/R/0001 .....	9
2.12.2.	ChondroCelect – Characterised viable autologous cartilage cells expanded in vivo expressing specific marker proteins; EMA/H/C/00878/MEA 16.4. 18.4 .....	9
<b>3.</b>	<b>Certification of ATMPs</b>	<b>9</b>
3.1.	New applications .....	9
3.2.	Day 60 evaluation reports .....	9
3.3.	Opinions .....	9

<b>4.</b>	<b>Scientific Recommendation on Classification of ATMPs</b>	<b>10</b>
4.1.	<b>New requests – appointment of CAT Co-ordinators</b>	<b>10</b>
4.1.1.	Allogeneic mesenchymal precursor cells	10
4.1.2.	<i>In vitro</i> expanded autologous articular chondrocytes	10
4.1.3.	Autologous cells of stromal vascular fraction (SVF) of adipose tissue	10
4.1.4.	Decellularised trachea seeded with autologous expanded mesenchymal stem cells (MSCs)	10
4.1.5.	Autologous mesenchymal stem cells isolated from bone marrow or adipose tissue; allogeneic mesenchymal stem cells from umbilical cord	11
4.2.	<b>Day 30 Co-ordinators’ first reports</b>	<b>11</b>
4.2.1.	hESC-derived Hepatocyte like cells	11
4.2.2.	Live-attenuated, double-delete <i>Listeria monocytogenes</i> expressing human mesothelin	11
4.2.3.	Allogeneic hematopoietic progenitor cells (HPC–CD34+) accompanied by facilitating cells (FC– CD8+/αβTCR-) and αβ T cells, prepared from mobilized peripheral blood mononuclear cells.	11
4.2.4.	Encapsulated allogeneic cells genetically modified to secrete GM-CSF and irradiated autologous tumour cells	12
4.3.	<b>Finalisation of procedures</b>	<b>12</b>
4.4.	<b>Follow-ups and guidance</b>	<b>12</b>
<b>5.</b>	<b>Scientific Advice</b>	<b>12</b>
5.1.	<b>New scientific advices – appointment of CAT Rapporteur</b>	<b>12</b>
5.2.	<b>CAT Rapporteurs’ reports</b>	<b>12</b>
5.3.	<b>Lists of issues</b>	<b>12</b>
5.4.	<b>Finalisation of Scientific Advice procedures</b>	<b>12</b>
<b>6.</b>	<b>Pre-Authorisation Activities</b>	<b>12</b>
6.1.	<b>Paediatric investigation plans (PIP)</b>	<b>12</b>
6.2.	<b>ITF briefing meetings in the field of ATMPs</b>	<b>12</b>
<b>7.</b>	<b>Organisational, regulatory and methodological matters</b>	<b>13</b>
7.1.	<b>Mandate and organisation of the CAT</b>	<b>13</b>
7.1.1.	CAT membership	13
7.1.2.	CAT minutes	13
7.2.	<b>Coordination with EMA Scientific Committees</b>	<b>13</b>
7.2.1.	Committee for Medicinal Products for Human Use (CHMP)	13
7.3.	<b>Coordination with EMA Working Parties/Working Groups/Drafting Groups</b>	<b>13</b>
7.3.1.	Good Laboratory Practice (GLP) requirements of non-clinical studies for ATMPs	13
7.3.2.	Pharmacovigilance: GVP Module P.II Biologicals	13
7.3.3.	Adaptive pathway initiative (formerly known as adaptive licensing)	14
7.3.4.	ADAPT SMART (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes)	14

7.3.5.	EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP).....	14
7.3.6.	Questions and Answers on minimally manipulated ATMPs .....	14
<b>7.4.</b>	<b>Co-operation within the EU regulatory network.....</b>	<b>15</b>
7.4.1.	Analysis of European Clinical Trials Database (EudraCT) .....	15
7.4.2.	Guideline on requirements for investigational ATMPs .....	15
7.4.3.	GMP requirements for ATMPs .....	15
<b>7.5.</b>	<b>Co-operation with international regulators.....</b>	<b>16</b>
7.5.1.	International Pharmaceutical Regulators Forum (IPRF), New Orleans (USA), 13-16 May 2015 .....	16
7.5.2.	Health Canada: guideline on 'cell therapy products in clinical trials'.....	16
7.5.3.	Update on recent confidentiality arrangements with third country regulators and organisations .....	16
<b>7.6.</b>	<b>CAT Work Plan .....</b>	<b>16</b>
7.6.1.	CAT Work Plan 2016 .....	16
7.6.2.	CAT-ISCT Joint Workshop: 'Challenges and opportunities for the successful development and approval of advanced therapy medicinal products', Seville (Spain), Friday 25th September 2015, 14:15 – 18:45.....	17
<b>7.7.</b>	<b>Planning and reporting .....</b>	<b>17</b>
<b>7.8.</b>	<b>Others .....</b>	<b>17</b>
7.8.1.	International Society for Stem Cell Research (ISSCR): Guidelines for stem cell science and clinical transformation .....	17
7.8.2.	Society for Immunotherapy on Cancer (SITC): chapters for a textbook on 'Cancer immunotherapy' .....	17
7.8.3.	Alliance for Regenerative Medicine: Stem Cell Conference 2015, 7-9 October, 2015, La Jolla, Mesa, CA, USA. ....	18
<b>8.</b>	<b>Any other business</b>	<b>18</b>
<b>9.</b>	<b>Explanatory notes</b>	<b>19</b>

## **1. Introduction**

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

List of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CAT plenary session held on 17-18 September 2015. See September 2015 CAT minutes (to be published post October 2015 CAT meeting).

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 agenda was adopted.

### **1.3. Adoption of the minutes of the July 2005 meeting**

The minutes were adopted and will be published on the EMA website.

### **1.4. August Written Procedure**

Report of the August 2015 Written Procedure was noted.

## **2. Evaluation of Advanced Therapy Medicinal Products**

### **2.1. Opinions**

None

## 2.2. Oral explanations

### 2.2.1. Talimogene laherparepvec; EMA/H/C/0002771

---

Treatment of adults with melanoma that is regionally or distantly metastatic

Scope: Oral explanation and report from the SAG oncology

**Action:** Oral explanation held on 17.09.2015 at 17:00hrs

Documents:

SAG report

SAG List of Participants

BWP report

The SAG Vice-chair presented to CAT the report of the SAG oncology meeting. Further to the oral explanation to the CAT, CAT adopted a second list of outstanding issues. CAT adopted the evaluation timetable.

## 2.3. D180 List of outstanding issues (LoOIs)

None

## 2.4. D120 Lists of questions (LoQs)

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

---

GlaxoSmithKline Trading Services - UK; treatment of children aged 0-18 diagnosed with ADA-SCID and for whom no suitable HLA-identical sibling bone marrow donor is available

Scope: Day 120 list of questions

**Action:** for adoption

Documents:

BWP report

Draft list of question

Notes:

CAT granted an accelerated assessment in April 2015

The Rapporteur presented the draft list of questions. The BWP report was discussed: CAT agreed with the BWP position. CAT adopted the list of questions and the evaluation timetable.

## 2.5. Day 80 assessment reports

None

## 2.6. Re-examination procedure (new applications) under Article 9(2) of Regulation No. 726/2004

### 2.6.1. Heparesc - Allogeneic human heterologous liver cells; *Orphan*; EMA/H/C/003750

---

Cytonet GmbH & Co. KG; treatment of urea cycle disorders (UCD) Scope: re-examination of the Opinion and consultation of ad-hoc expert group **Action:** for adoption

Documents:

Draft List of Questions to the ad-hoc expert group  
Preliminary list of experts for endorsement by CAT

Ad-hoc expert group expertise required:

- Paediatrician and/or paediatric intensive care specialist with expertise in urea cycle disorders
- Paediatrician hepatologist with expertise in liver genetic diseases
- Surgeon with expertise in paediatric liver surgery
- Preclinical lab specialist with expertise in urea cycle disorders

Note:

The CAT adopted in April 2015 a negative draft Opinion.

The CHMP adopted in June 2015 a negative Opinion.

The re-examination Rapporteur presented to CAT the list of questions to the ad-hoc expert group. The list of questions was discussed and amendments were proposed by the CAT members. The amended list of questions was adopted.

CAT agreed with the preliminary list of experts for the ad hoc group meeting. The final list will be adopted via a written procedure at the end of nomination period.

## 2.7. Withdrawal of initial full application

None

## 2.8. Ongoing initial full application

None

## 2.9. New applications

### 2.9.1. Expanded adipose-derived stem cells of allogeneic origin; *Orphan*; EMA/H/C/0004258

---

TiGenix S.A.U.; Intended for the treatment of complex perianal fistulas in adult patients

Scope: Rapporteur & Peer reviewer nominations

**Action:** for information

Note:

The CHMP granted at its June 2015 plenary eligibility as a centralised product under Art. 3(1) Indent 1a ATMP Regulation (EC) 126/2004

## 2.10. GMP and GCP inspections requests

None

## 2.11. Type II variations

### 2.11.1. Glybera – Alipogene tiparvovec; *Orphan*; EMA/H/C/002145/II/34

---

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Scope: Update of section 5.1 of the SmPC based on the final clinical study report (CSR) for Study CT-AMT-011-02

**Action:** for adoption

Draft opinion

The draft opinion was adopted.

#### 2.11.2. Glybera – Alipogene tiparvec; Orphan; EMA/H/C/002145/II/37-G

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to reflect new safety and efficacy data from CSR for Study 011-01

**Action:** for adoption

Draft opinion

The draft opinion was adopted.

#### 2.11.3. Glybera – Alipogene tiparvec; Orphan; EMA/H/C/002145/II/38

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Scope: Update of sections 4.4 and 5.1 of the SmPC based on the final CSR for Study CT-AMT-011-05

**Action:** for adoption

Draft opinion

CAT discussed the proposed wording for the update of section 5.1 of the product information. Following agreement by the MAH, CAT adopted the draft opinion.

#### 2.11.4. Glybera – Alipogene tiparvec; Orphan; EMA/H/C/002145/II/46-G

UniQure Biopharma B.V.

Rapporteur: C. Niederlaender; CHMP Coordinators: G. Markey

Scope: changes to manufacturing process of the active substance (grouped variation) to introduce a viral clearance nanofiltration step.

**Action:** for adoption

RSI

CAT adopted the RSI and the evaluation timetable.



## 2.12. Other post-authorisation activities

### 2.12.1. Holoclar – *Ex vivo* expanded autologous human corneal epithelial cells containing stem cells; *Orphan*; EMA/H/C/002450/R/0001

---

Chiesi Farmaceutici S.p.A.; treatment of adult patients with moderate to severe limbal stem cell deficiency

Rapporteur: E. Flory, CAT Co-Rapporteur: P. Gasparini; CHMP Coordinator: J. Mueller-Berghaus

**Scope:** Conditional Renewal - timetable

**Action:** for adoption

Note: conditional MA adopted in December 2014

CAT adopted the timetable for the conditional renewal.

### 2.12.2. ChondroCelect – Characterised viable autologous cartilage cells expanded in vivo expressing specific marker proteins; EMA/H/C/00878/MEA 16.4. 18.4

---

TiGenix N.V.

Scope 16.4: Randomised control trial protocol TIG/ACT/04/2009

Scope 18.4: Non-interventional registry of ChondroCelect, Study TGX001-2011 & randomised controlled study in small lesions using microfracture as comparator

Rapporteur: Egbert Flory; Co-rapporteur: Tiina Palomäki; CHMP Coordinators: Jan Müller-Berghaus

**Action:** for information

CAT noted the timetable (adopted in June 2015).

## 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. New applications

### 3.2. Day 60 evaluation reports

None

### 3.3. Opinions

None

## 4. Scientific Recommendation on Classification of ATMPs

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

#### 4.1.1. Allogeneic mesenchymal precursor cells

---

Intended for the treatment of chronic lumbar back pain

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

**Action:** for adoption

Request received 20<sup>th</sup> August 2015

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

#### 4.1.2. *In vitro* expanded autologous articular chondrocytes

---

Intended for the treatment of articular cartilage defect

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

**Action:** for adoption

Request received 18<sup>th</sup> August 2015

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

#### 4.1.3. Autologous cells of stromal vascular fraction (SVF) of adipose tissue

---

Intended for (1) cosmetic lipofiling; (2) treatment for non-healing wounds and scared tissue; (3) treatment of osteoarthritis in the knee

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

**Action:** for adoption

Request received 27<sup>th</sup> August 2015

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

#### 4.1.4. Decellularised trachea seeded with autologous expanded mesenchymal stem cells (MSCs)

---

Intended for the treatment of reconstruction of trachea subsequent to damage or stenosis due to cancer, injury, infection or congenital deformities

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

**Action:** for adoption

Request received 3<sup>rd</sup> September 2015

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

#### 4.1.5. Autologous mesenchymal stem cells isolated from bone marrow or adipose tissue; allogeneic mesenchymal stem cells from umbilical cord

---

Intended for the treatment of amyotrophic lateral sclerosis

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

**Action:** for adoption

Request received 3<sup>rd</sup> September 2015

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

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

### 4.2.1. hESC-derived Hepatocyte like cells

---

Intended for the treatment of inborn errors of liver metabolism diseases and liver acute failure.

**Action:** for adoption

Classification report

CAT discussed the ATMP classification report prepared by the CAT coordinator and decided to request some additional information from the applicant prior to concluding on this classification request. The request for supplementary information was adopted.

### 4.2.2. Live-attenuated, double-delete *Listeria monocytogenes* expressing human mesothelin

---

Intended for the treatment of malignant pleural mesothelioma.

**Action:** for adoption

Classification report

CAT discussed the ATMP classification report. CAT adopted by consensus the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the Commission for comments until 2 October 2015.

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.

### 4.2.3. Allogeneic hematopoietic progenitor cells (HPC-CD34+) accompanied by facilitating cells (FC- CD8+/ $\alpha\beta$ TCR-) and $\alpha\beta$ T cells, prepared from mobilized peripheral blood mononuclear cells.

---

Intended for the prophylaxis of organ rejection in adult patients receiving living donor kidney transplantation.

**Action:** for adoption

Classification report

CAT discussed the ATMP classification report prepared by the CAT coordinator and decided to request some additional information from the applicant prior to concluding on this classification request. The request for supplementary information was adopted.

#### 4.2.4. Encapsulated allogeneic cells genetically modified to secrete GM-CSF and irradiated autologous tumour cells

---

Intended for the treatment of advanced solid tumours.

**Action:** for adoption

Classification report

CAT discussed the ATMP classification report. CAT adopted by consensus the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the Commission for comments until 2 October 2015.

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.

#### 4.3. Finalisation of procedures

None

#### 4.4. Follow-ups and guidance

None

### 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 scientific advices – appointment of CAT Rapporteur

#### 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

None

## 7. Organisational, regulatory and methodological matters

### 7.1. Mandate and organisation of the CAT

#### 7.1.1. CAT membership

---

Denmark: Sinan B. Sarac - termination of mandate for member

**Action:** for information

The information was noted.

#### 7.1.2. CAT minutes

---

Scope: Rolling minutes as a working tool for CAT members

**Action:** for information

The information was noted.

### 7.2. Coordination with EMA Scientific Committees

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

---

Summary of Outcomes (SoO) for the July 2015 meeting

**Action:** for information

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

#### 7.3.1. Good Laboratory Practice (GLP) requirements of non-clinical studies for ATMPs

---

CAT resources: U. Riekstina, T. Palomäki, E. Flory, C. Herberts (Netherlands), I. Vieira (Portugal)

**Action:** for discussion

Note:

June 2015: presentation by the EMA GLP IWP on GLP requirements for ATMPs

July 2015: CAT agreed on the composition of a drafting group to draft a document summarising experiences and expectation in relation to the GLP requirements of non-clinical studies of ATMP

17-18 September 2015: discussion of the observations made by the CAT drafting group members

15-16 October 2015: joint discussion with the GLP Inspections Working Party (IWP) to agree on a common position

This topic was postponed to the October CAT meeting. The interaction with the GLP inspectors will also be postponed until after the CAT discussion.

#### 7.3.2. Pharmacovigilance: GVP Module P.II Biologicals

---

**Action:** for discussion

Document:

Module

Note: this module is presented to committees for discussion and comments before a public consultation.

The draft GVP Module P. II Biologicals was presented. CAT member will review the document and provide input on behalf of the CAT. It was mentioned that BWP will also provide feedback (especially on the question what would be significant manufacturing changes that would require an update of the RMP).

A general comment was made that it should be kept in mind not to increase the regulatory burden for ATMP MAHs: it is not appropriate to impose the same requirements as for MAHs of biologicals (that are produced on large batch sizes).

### 7.3.3. Adaptive pathway initiative (formerly known as adaptive licensing)

CAT resources: Hans Ovelgönne

Scope: presentation of the procedure and experience with ATMPs under discussion in the Adaptive Pathway initiative

**Action:** for information

Further information can be found

here: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000601.jsp&mid=WC0b01ac05807d58ce](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp&mid=WC0b01ac05807d58ce)

Topic postponed until the October CAT meeting.

### 7.3.4. ADAPT SMART (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes)

EMA resources: Hans-Georg Eichler, EMA's Senior Medical Officer

**Action:** for information

Further information can be found here:

<http://adaptsmart.eu/press-release-innovative-medicines-initiative-launches-adapt-smart-an-adaptive-pathways-project-with-32-international-participants/>

EMA's senior medical officer presented the ADAPT-SMART projects are asked if CAT members would be interested to be part in the 3 Work packages (WP) of this project. CAT members expressed their interest to contribute to the different WP as reviewers.

### 7.3.5. EMA Human Scientific Committees' Working Parties with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP)

Scope: PCWP plenary meeting held on 03 June 2015

Scope: PCWP/HCPWP joint meeting held on 04 June 2015

Scope: HCPWP meeting held on 04 June 2015

**Action:** for information

Documents:  
Minutes

The information was noted.

### 7.3.6. Questions and Answers on minimally manipulated ATMPs

CAT drafting group: M. Lipnik Stangelj (Rapp), P. Salmikangas (Rapp), T. Palomäki, E. Flory, M. Menezes Ferreira, P. Doevendans, M. Hrubisko

Scope: to create a Q&A document following the discussion that took place at the CAT-CHMP joint Strategic Review & Learning meeting in May 2015

**Action:** for information

Feedback was provided from the breakout meeting that took place on Wednesday 16 September 2015. The drafting group members will develop completed risk-based approach (RBA) tables for three different types of minimally manipulated ATMPs and on basis of these examples explain (in the Q&A) how to use the RBA for such products.

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

### 7.4.1. Analysis of European Clinical Trials Database (EudraCT)

---

CAT resources: M. Menezes-Ferreira, I. Reischl, T. Boráň, P. Salmikangas, N. Ferry, R. Mačiulaitis, D. Śladowski, M. Lipucci di Paola, B. Gänsbacher

Scope: Analysis of EudraCT for trials with ATMPs

**Action:** for discussion

Feedback was provided from the breakout meeting that took place on Wednesday 16 September 2015. Further analysis will be done by the CAT Drafting group (DG) members and figures/data will be presented at the October CAT meeting. The DG members will work in parallel on a publication of these results.

### 7.4.2. Guideline on requirements for investigational ATMPs

---

CAT drafting groups for investigational gene therapy and cell-based medicinal products: T. Palomäki (Rapporteur), I. Reischl (Rapp), M. Lipnik-Stangelj, M. Menezes Ferreira, M. O'Donovan, N. Ferry, S. Badoi, T. Boráň, C. Niederlaender

**Action:** for information

Feedback was provided from the breakout meeting that took place on Wednesday 16 September 2015.

The guideline will address the requirement for clinical trials with gene and cell therapy products for early and late phase clinical trials. The Guideline will incorporate the existing Guideline on 'Non-clinical studies required before first clinical use of gene therapy medicinal products' (CHMP/GTWP/125459/06). A (virtual) drafting group (DG) meeting will take place before the November CAT meeting.

It was mentioned that content of this guideline could be a good topic for the Strategic Review & Learning Meeting that will be held in the Netherlands in the first half of 2016 (joint meeting with the PDCO and CTFG).

### 7.4.3. GMP requirements for ATMPs

---

Scope: European Commission consultation document has been released for external consultation: [http://ec.europa.eu/health/files/advtherapies/2015\\_pc/publ\\_cons\\_doc\\_2015.pdf](http://ec.europa.eu/health/files/advtherapies/2015_pc/publ_cons_doc_2015.pdf)

**Action:** for information

Note: the draft GMP requirements for ATMPs (developed by CAT and the GMP inspectors) were published on the Commission website for external consultation until November 2015.

The Commission representative provided information on published consultation paper and the next steps after the comments from the external stakeholders. The Commission asked the CAT and the GMP inspectors working group to continue assisting the Commission to finalise the GMP guide for ATMPs. CAT members were also asked to disseminate the GMP concept paper to ATMP developers in universities and hospitals in order to get their comments.

## 7.5. Co-operation with international regulators

### 7.5.1. International Pharmaceutical Regulators Forum (IPRF), New Orleans (USA), 13-16 May 2015

---

CAT resources: Nicolas Ferry

Scope: Feedback on IPRF Cell Therapy and Gene Therapy Groups

Scope: Feedback from the IPRF - Gene Therapy Working Group meeting

**Action:** for information

Feedback was given to the CAT members on the activities of the IPRF working groups and of the outcome of the in-person meeting of the IPRF-GTWG in New Orleans.

### 7.5.2. Health Canada: guideline on 'cell therapy products in clinical trials'

---

Scope: guideline on quality, non-clinical and clinical requirement for applications for early and late clinical trials

**Action:** for information

The guideline was noted.

### 7.5.3. Update on recent confidentiality arrangements with third country regulators and organisations

---

**Action:** for information

Note: CAT was informed that two confidentiality arrangements have been concluded by the European Commission DG SANTE and EMA in July and September 2015 respectively; the first with Swissmedic and the second with the WHO. Both arrangements are concluded for an initial period of 5 years, and may be renewed. Confidentiality agreements were already in place between EMA and the following international partners: US FDA, Japan PMDA/MHLW, Health Canada and TGA Australia.

Under the terms of confidentiality or working arrangements, the parties to the arrangement agree not to disclose non-public information, which means that product related information can be shared between the parties. The arrangements also facilitate ad hoc participation at product related discussions in response to specific requests.

The information was noted.

## 7.6. CAT Work Plan

### 7.6.1. CAT Work Plan 2016

---

Scope: identification of projects and CAT topic leaders and participants for the different topics

CAT resources: Paula Salmikangas

**Action:** for discussion



The CAT topics for the workplan 2016 were presented and discussed. CAT topic leaders and CAT contributors were identified. The CAT workplan 2016 will be updated with this information and presented to the CAT in October 2015 for further discussion / agreement.

#### 7.6.2. CAT-ISCT Joint Workshop: 'Challenges and opportunities for the successful development and approval of advanced therapy medicinal products', Seville (Spain), Friday 25th September 2015, 14:15 – 18:45

---

CAT resources: Paula Salmikangas

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2015/06/news\\_detail\\_002357.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/06/news_detail_002357.jsp&mid=WC0b01ac058004d5c1)

**Action:** for information

The information was noted.

### 7.7. Planning and reporting

None

### 7.8. Others

#### 7.8.1. International Society for Stem Cell Research (ISSCR): Guidelines for stem cell science and clinical transformation

---

Scope: review of ISSCR's Guidelines for stem cell science and clinical transformation

**Action:** for discussion

Note:

The draft guideline covers many fields starting from sourcing and manufacturing, non-clinical studies, ethical issues and clinical trials in early and late development, use in clinical care setting, access and economic question.

Comments received from the consulted committees and working parties/groups were discussed during the September 2015 CAT plenary meeting and CHMP Orgam meeting. These comments, together with the additional observations made by the CAT will be consolidated in a formal EMA response to ISSCR.

#### 7.8.2. Society for Immunotherapy on Cancer (SITC): chapters for a textbook on 'Cancer immunotherapy'

---

Scope: contribution by CAT members to the textbook

**Action:** for discussion and appointment of co-authors

Note: the chapters will address quality, non-clinical and clinical aspects of cell therapy, gene therapy and combination cancer immunology products; the fourth chapter deals with companion diagnostics / immune monitoring: four to five co-authors from CAT are sought for each chapter. Deadline for completion of the manuscripts: April 2016.

CAT members expressed interest to contribute to the chapters on gene therapy and cell therapy.

7.8.3. Alliance for Regenerative Medicine: Stem Cell Conference 2015, 7-9 October, 2015, La Jolla, Mesa, CA, USA.

---

CAT resources: Ján Kyselovič

Scope: cell therapy, gene therapy and tissue engineering sectors together with the academic research community to advance scientific discovery and commercial development. Ján Kyselovič will attend.

**Action:** for information

Note: <http://alliancerm.org/event/stem-cell-meeting-mesa>

The information was noted.

## 8. Any other business

## 9. Explanatory notes

The Notes give a brief explanation of relevant agenda items and abbreviations used. They should be read in conjunction with the agenda/minutes.

### 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  
GMP: Good Manufacturing Practice  
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  
PDCO: Paediatric Committee  
PIP: Paediatric Investigation Plan  
PL: Package leaflet  
PRAC: Pharmacovigilance and Risk Assessment Committee  
RSI: Request for supplementary information  
SA: Scientific Advice  
SAG-O: Scientific Advisory Group Oncology  
SAWP: Scientific Advice Working Party  
SmPC: Summary of Products Characteristics  
TT: Timetable

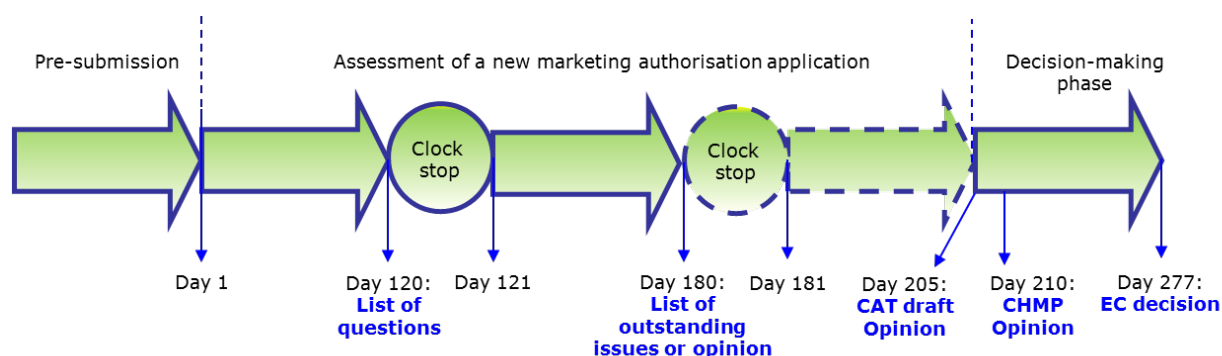
## Evaluation of ATMPs (section 2)

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 17–18 September 2015 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	
Martin Brunner	Alternate	Austria	No restrictions applicable to this meeting	
Claire Beuneu	Member	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Ivica Malnar	Alternate	Croatia	No restrictions applicable to this meeting	
Anna Paphitou	Member	Cyprus	No interests declared	
Tomáš Boráň	Member	Czech Republic	No interests declared	
Nanna Aaby Kruse	Alternate	Denmark	No restrictions applicable to this meeting	
Toivo Maimets	Member	Estonia	No interests declared	
Tarmo Tiido	Alternate	Estonia	No interests declared	
Tiina Palomäki	Member	Finland	No interests declared	
Olli Tenhunen	Alternate	Finland	No restrictions applicable to this meeting	
Nicolas Ferry	Member	France	No interests declared	
Violaine Closson	Alternate	France	No interests declared	
Martina Schüssler-Lenz	Member (Vice-Chair)	Germany	No interests declared	
Egbert Flory	Alternate	Germany	No interests declared	
Asterios Tsiftoglou	Member	Greece	No interests declared	
Balázs Sarkadi	Alternate	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Paolo Gasparini	Member	Italy	No interests declared	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No restrictions applicable to this meeting	
Guy Berchem	Alternate (to CHMP)	Luxembourg	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
	representative)			
Johannes Hendrikus Ovelgönne	Member	Netherlands	No interests declared	
Marit Hystad	Member	Norway	No interests declared	
Rune Kjekken	Alternate	Norway	No restrictions applicable to this 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	
Lennart Åkerblom	Member	Sweden	No interests declared	
Christiane Niederlaender	Member	United Kingdom	No interests declared	
Esteve Trias-Adroher	Alternate	Healthcare Professionals' Representative	No interests declared	
Bernd Gänsbacher	Member	Healthcare Professionals' Representative	No interests declared	
Michelino Lipucci di Paola	Member	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member	Patients' Representative	No restrictions applicable to this meeting	
Guido Panté	Expert - in person*	Italy	No interests declared	
Wiebke Hoppensack	Expert - via telephone*	Germany	No restrictions applicable to this meeting	
Ingrid Wang	Expert - via	Norway	No interests declared	



Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-Dol	Topics on agenda for which restrictions apply
	telephone*			
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Karri Penttila	Expert - via telephone*	Finland	No interests declared	
Louise Bisset	Expert - via telephone*	UK	No interests declared	
Riaz Zuhrie	Expert - via telephone*	UK	No interests declared	
Tanya Chambers	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.