



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

4 October 2023  
EMA/CAT/412887/2023  
Human Medicines Division

## Committee for Advanced Therapies (CAT)

Minutes of the meeting on 06-08 September 2023

Chair: Ilona Reischl; Vice-Chair: Kieran Breen

### Disclaimers

Some of the information contained in these 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, these 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 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).



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## **1. Introduction**

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

The Chairperson opened the meeting by welcoming all participants. The meeting was held remotely.

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 on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants for agenda topics was identified.

Participants 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. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The Chair thanked the departing member from Hungary for her contributions to the Committee.

The EMA secretariat announced the names of the Committee members who delegated their vote via proxy and the Committee members who received such proxy.

### **1.2. Adoption of agenda**

The CAT agenda for 06-08 September 2023 meeting was adopted.

### **1.3. Adoption of the minutes**

The CAT minutes of the 12-14 July 2023 and 09-11 August (by written procedure) meetings were adopted.

## **2. Evaluation of ATMPs**

### **2.1. Opinions**

No items

### **2.2. Oral explanations**

No items

## 2.3. Day 180 list of outstanding issues

### 2.3.1. Exagamglogene autotemcel - PRIME - Orphan - EMEA/H/C/005763

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Vertex Pharmaceuticals (Ireland) Limited; Treatment of transfusion-dependent  $\beta$ -thalassemia and sickle cell disease

Scope: Day 180 list of outstanding issues

**Action:** for adoption

List of questions adopted on 17.05.2023.

The Rapporteur presented the outcome of the assessment of responses to the list of questions. Feedback was provided from the discussions in the Biologics Working Party.

The list of outstanding issues was adopted.

## 2.4. Day 120 list of questions

### 2.4.1. Fidanacogene elaparvovec - PRIME - Orphan - EMEA/H/C/004774

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Pfizer Europe MA EEIG; Indicated for the treatment of severe and moderately severe haemophilia B

Scope: Day 120 list of questions

**Action:** for adoption

The Rapporteur and CoRapporteur presented the outcome of the assessment of the marketing authorisation application. The outcome of the quality assessment was also discussed in the Biologics Working Party

The list of questions was adopted.

## 2.5. Day 80 assessment reports

No items

## 2.6. Update on ongoing initial applications

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. Companion diagnostics

### 2.10.1. Initial consultation

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No items

### 2.10.2. Follow-up consultation

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No items

## 2.11. Type II variations and variations of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

### 2.11.1. Alofisel - darvadstrocel - Orphan - EMEA/H/C/004258/II/0044/G

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Takeda Pharma A/S

Rapporteur: Maria Luttgen

Scope: Safety, Opinion

Grouped application comprising one type II variation and two type IB as follows:

- Update of section 4.8 of the SmPC in order to update the summary of the safety profile and to add anal abscess, proctalgia and anal fistula to the list of adverse drug reactions on post-marketing experience following the assessment of R/0036 based on a review of the MAH's Global Safety Database.
- Update of section 4.2 of the SmPC in order to add the term Perilesional as an EDQM term, following the assessment of R/0036.
- Update of sections 1, 2.2, 3, 4.2, 6.5 and 6.6 of the SmPC in order to replace the term "suspension for injection" for "dispersion for injection", following the assessment of R/0036. The Annex A, Package Leaflet and Labelling are updated in accordance.

**Action:** for adoption

Request for supplementary information adopted on 17.05.2023.

The Rapporteur presented the outcome of the assessment and the changes that were implemented to the product information. The opinion was adopted.

### 2.11.2. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0003

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli



Scope: Quality, Opinion

**Action:** for adoption

Request for supplementary information adopted on 07.10.2022 and 15.07.2022.

The opinion was adopted.

### 2.11.3. [Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0014](#)

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, PRAC Rapporteur: Gabriele Maurer

Scope: Clinical, Opinion

Update of section 5.1 of the SmPC in order to update efficacy information based on final results from studies 017001 and JCAR-017-BCM-001 listed as obligations in the Annex II. These studies aimed to further characterise the long-term efficacy and safety of Breyanzi in patients treated with relapsed or refractory DLBCL, PMBCL, FL3B after two or more lines of systemic therapy. Study 017001 is a phase 1, open-label, single-arm, multicohort, multicentre, seamless design trial, while study JCAR-017-BCM-001 is a phase 2, open-label, single-arm, multicohort, multicentre trial. The Annex II is updated accordingly. The RMP version 3.0 has also been submitted.

**Action:** for adoption

Request for supplementary information adopted on 24.03.2023.

The Rapporteur presented the outcome of the assessment and the changes that were implemented to the product information. The opinion was adopted.

### 2.11.4. [Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0021](#)

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, Opinion

**Action:** for adoption

Request for supplementary information adopted on 14.07.2023.

The opinion was adopted.

### 2.11.5. [Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0026/G](#)

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli

Scope: Quality, Request for supplementary information

**Action:** for adoption

The request for supplementary information was adopted.

#### 2.11.6. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/II/0021

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays

Scope: Clinical, Request for supplementary information

Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 1 prior therapy, including an immunomodulatory agent (IMiD) and a protease inhibitor (PI), have demonstrated disease progression on or after the last therapy and are refractory to lenalidomide for CARVYKTI, based on interim results from study MMY3002 listed as a specific obligation (SOB/006) in the Annex II. This is an ongoing, Phase 3, randomised, open-label, multicentre study to determine whether treatment with cilta-cel provides an efficacy benefit compared to standard therapy in participants with relapsed and lenalidomide-refractory multiple myeloma. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II of the product information (PI). As part of the application the MAH is requesting a 1-year extension of the market protection.

**Action:** for adoption

The Rapporteur presented the evaluation of this application for extension of indication to a second line setting.

The request for supplementary information was adopted.

#### 2.11.7. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0063

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen

Scope: Clinical, Opinion

Submission of the final report from study 20110261 listed as a category 3 study in the RMP. This is a Phase I, multi-centre, open-label, dose de-escalation study to evaluate the safety and efficacy of talimogene laherparepvec in paediatric subjects with advanced noncentral nervous system tumours that are amenable to direct injection.

**Action:** for adoption

The final report of the study 20110261 did not result in new safety issues and the benefit risk profile is unchanged. There are no changes to the product information. The opinion was adopted.

#### 2.11.8. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0064

Amgen Europe B.V.

Rapporteur: Maija Tarkkanen, PRAC Rapporteur: Gabriele Maurer

Scope: Safety, Opinion

Submission of an updated RMP version 11.0 in order to remove the important potential risk of 'talimogene laherparepvec-mediated anti-GM-CSF antibody response', based on the accumulated scientific and clinical data.

**Action:** for adoption

The opinion was adopted.

#### 2.11.9. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0072

Novartis Europharm Limited

Rapporteur: Rune Kjekken

Scope: Quality, Request for supplementary information

**Action:** for adoption

The request for supplementary information was adopted.

#### 2.11.10. Libmeldy - atidarsagene autotemcel - Orphan - EMEA/H/C/005321/II/0015

Orchard Therapeutics (Netherlands) B.V.

Rapporteur: Johannes Hendrikus Ovelgonne

Scope: Quality, Opinion

**Action:** for adoption

Request for supplementary information adopted on 16.06.2023.

The opinion was adopted.

#### 2.11.11. Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352/II/0013

PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: Quality, Request for supplementary information

**Action:** for adoption

The Rapporteur presented the outcome of the assessment of this variation.

The request for supplementary information was adopted.

### 2.11.12. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0040

Novartis Europharm Limited

Rapporteur: Johannes Hendrikus Ovelgonne, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Safety, Opinion

Update of sections 4.4 and 5.1 of the SmPC in order to add a new warning and precaution capturing the theoretical risk of tumorigenicity as a result of vector integration and to include a new statement indicating random instances of vector integration are possible based on final results from studies 2220205 and 2220117, and literature. The Package Leaflet is updated accordingly. The RMP version 3 has also been submitted.

**Action:** for adoption

Request for supplementary information adopted on 14.07.2023.

The opinion was adopted.

## **2.12. Extension applications**

No items

## **2.13. Other Post-Authorisation Activities**

### 2.13.1. CARVYKTI - ciltacabtagene autoleucel - Orphan - EMEA/H/C/005095/MEA/007.2

Janssen-Cilag International NV

Rapporteur: Jan Mueller-Berghaus

Scope: Pharmacovigilance, Opinion

MAH Response to MEA 007.1 [Study no: PCSONCA0014] as adopted in April 2023:  
The MAH should target a minimum enrolment of 30 healthcare professionals (HCPs) in each role (physicians, nurses, pharmacists) to allow valid statistical analysis. The MAH should make sure that there are at least 30 HCPs in each role and continue to enrol centres until this target is achieved [From Initial MAA]

**Action:** for adoption

The Rapporteur's assessment of the post-authorisation measure was adopted.

### 2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/LEG/021

Novartis Europharm Limited

Rapporteur: Rune Kjekken

Scope: Pharmacovigilance, Request for supplementary information

From EMEA/H/C/PSUSA/00010702/202208:

MAH's responses to supplementary information.

List of issues relates to potential secondary malignancy cases (PSUR 07 (reporting period

13-Aug-2021 to 12-Aug-2022))

**Action:** for adoption

The Rapporteur's assessment of the post-authorisation measure was adopted.

### 2.13.3. [Upstaza - eladocagene exuparvovec - Orphan - EMEA/H/C/005352](#)

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PTC Therapeutics International Limited

Rapporteur: Maura O'Donovan

Scope: EMA updates on the interaction with iNTD, as a possible data source for Upstaza SOB PTC-AADC-MA-406

**Action:** for discussion

This is an update on post-authorisation measure MEA/007 (discussed at the March 2023 CAT meeting, agenda point 2.13.7). EMA provided feedback on the interaction with the iNTD registry holder, during which the expectations from EMA for a registry holder were clarified. CAT agreed for EMA to organise a meeting with the marketing authorisation holder and the registry holder.

CAT suggested to make an information package to explain what is expected from registry holders when involved in post-authorisation studies for ATMPs. This can potentially be included in the revision of the GVP module 5.

## 2.14. **GMP and GCP inspections requests**

No items

## 3. **Certification of ATMPs**

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

### 3.1. **Opinion**

No items

### 3.2. **Day 60 Evaluation Reports**

No items

### 3.3. **New Applications**

No items

## 4. Scientific Recommendation on Classification of ATMPs

Timetable:

-Start of the procedure:	08.09.2023
-EMA Coordinator's draft report:	19.09.2023
-CAT Coordinator's comments:	27.09.2023
-Revised scientific recommendation:	29.09.2023
-CAT's discussion of scientific recommendation:	06.10.2023

### 4.1. New requests – Appointment of CAT Coordinator

#### 4.1.1. Devitalized cell-derived cartilaginous tissue

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Bone substitute for maxillofacial and/or orthopaedic bone defects

Scope: Appointment of CAT Coordinator and adoption of timetable

**Action:** for adoption

The CAT coordinator was appointed.

### 4.2. Day 30 ATMP scientific recommendation

#### 4.2.1. Allogeneic ex-vivo expanded pluripotent stem cell-derived cardiac ventricular progenitor cells

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Intended for the treatment of chronic and acute heart disease  
Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22.09.2023.

#### 4.2.2. Allogeneic ex-vivo expanded pluripotent stem cell-derived photoreceptor progenitor cells

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Intended for the treatment of retinitis pigmentosa

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22.09.2023.

#### 4.2.3. Allogeneic genetically modified human induced pluripotent stem cell-derived retinal pigment epithelial cells

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Intended for the treatment of Stargardt indication

Scope: ATMP scientific recommendation

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**Action:** for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22.09.2023.

#### 4.2.4. Autologous cultured fibroblasts

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Intended for the treatment of scars and wounds

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22.09.2023.

#### 4.2.5. Secretome (conditioned medium) from donor bone marrow mesenchymal stem cells (MSCs) containing cytokines, growth factors, proteins and extracellular vesicles

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Intended for the treatment of paediatric respiratory diseases called childhood interstitial lung disease (ChILD)

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 22.09.2023

### 4.3. Day 60 revised scientific recommendation (following list of questions)

No items

### 4.4. Finalisation of procedure

No items

### 4.5. Follow-up and guidance

#### 4.5.1. Cells treated by extracorporeal photopheresis

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CAT: Nancy De Bremaeker

Scope: Informal classification discussion on request of a member state

**Action:** for discussion

CAT discussed the question if the manipulation of (autologous) blood cells by extracorporeal photopheresis with psoralenes (8-MOP) and UV should be considered a substantial manipulation, and whether the treated cells should be considered as ATMPs.

CAT did recap the discussion in 2012, where it became clear that, at that time, there was no uniform classification in the EU. This was confirmed in a recent survey (conducted by the French authorities for tissues and cells and the European Commission, DG Santé of 22.04.2021) on Extracorporeal Chemotherapy procedures: in the majority of member states, such procedures were rather considered under the tissue and cell legislation (Directive 2004/23/EC). CAT members indicated the treatment with 8-MOP will mainly kill susceptible cells. It will also be very challenging or impossible to quality control the cells before being re-administered to the patient.

In absence of a harmonised classification of such products in the EU, the national authority might consider, as a pragmatic approach, to regulate these products under the tissue and cell legislation. That approach will also allow for products to be produced in a tissue establishment (TE) in one member state and transported to a TE in another member state.

## 5. Scientific Advice

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 Rapporteurs

#### 5.1.1. Ongoing scientific advice procedures - Appointment of CAT Peer Reviewers

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Timetable:

- Start of procedure at SAWP:	28-31.08.2023
- Appointment of CAT Peer Reviewers:	06-08.09.2023
- SAWP first reports:	18.09.2023
- CAT Peer Reviewer comments (NC/C)	22.09.2023
- CAT Peer Reviewer comments (Q)	27.09.2023
- Discussion at SAWP:	25-28.09.2023
- Discussion at CAT and feedback to SAWP:	04-06.10.2023

#### 5.1.2. Scientific advice procedures starting at the next SAWP meeting

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Timetable:

- Start of procedure at SAWP:	25-28.09.2023
- Appointment of CAT Peer Reviewers:	04-06.10.2023
- SAWP first reports:	16.10.2023
- CAT Peer Reviewer comments (NC/C)	20.10.2023
- CAT Peer Reviewer comments (Q)	25.10.2023
- Discussion at SAWP:	23-23.10.2023
- Discussion at CAT and feedback to SAWP:	30-31.10.2023

### 5.2. Procedures discussed at SAWP – 1st reports, D40 JRs, LoIs

### 5.3. Finalisation of D70 procedures – feedback from the discussion meeting

No items



## 5.4. Final Advice Letters for procedures finalised the previous month

No items

## 6. Pre-Authorisation Activities

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

No items

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

### 6.3. Priority Medicines (PRIME) – Eligibility requests

#### 6.3.1. Month 0 - Start of the procedure

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Timetable for assessment:

Procedure start: 28-31.08.2023

SAWP recommendation: 28.09.2023

CAT recommendation: 06.10.2023

CHMP adoption of report and final recommendation: 12.10.2023

#### 6.3.2. Month 1 – Discussion of eligibility

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#### 6.3.3. Month 2 – Recommendation of eligibility

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No items

#### 6.3.4. Ongoing support

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No items

## 7. Organisational, regulatory and methodological matters

### 7.1. Mandate and organisation of the CAT

#### 7.1.1. CAT membership

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The Chair thanked Katalin Lenguel for her contribution as member for Hungary.

**Action:** for information

#### 7.1.2. Vote by proxy

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None

**Action:** for information

#### 7.1.3. CAT Strategic Review & Learning meeting (SRLM) under the Spanish presidency, 25-27 October 2023 Madrid (Spain)

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CAT: Sol Ruiz, Marcos Timon

Scope: Topics for discussion at the upcoming SRLM

**Action:** for discussion

The latest version of the agenda of the SRLM was presented. CAT members can send additional topics for the agenda to the Spanish delegation.

#### 7.1.4. CAT 15<sup>th</sup> anniversary

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CAT: Ilona Reischl

Scope: CAT activities in 2024 related to its 15<sup>th</sup> anniversary

**Action:** for discussion

Note: the first meeting of CAT took place in January 2009

A fist reflection on specific activities for the 15<sup>th</sup> anniversary of the CAT took place.

It was agreed to include the 15-year activities in the CAT workplan for 2024 (see 7.6.1).

### 7.2. Coordination with EMA Scientific Committees

#### 7.2.1. Update from the PCWP-HCPWP

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Scope: Meeting summary of the PCWP-HCPWP that took place on 27 & 28 June 2023 and draft Agenda of the PCWP-HCPWP Joint meeting that will take place on 19 & 20 September 2023

**Action:** for information

The information was noted.

## 7.2.2. CAT-COMP working group meeting

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CAT: Ilona Reischl

Scope: Feedback from the CAT-COMP working group meeting that took place on 4 September 2023

**Action:** for information

Dariusz Sladowski and Maura O'Donovan provided a short feedback on the scientific and regulatory discussion that took place at the CAT-COMP working group meeting.

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

### 7.3.1. Patient Experience Data (PED) project

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Scope: PED community is to develop a reflection paper on the EU approach to collect and analyse PED and coordinate the actions agreed at the [workshop in Sep 2022](#).

**Action:** for information

CAT noted the presentation on the PED project. CAT members interested to participate in the develop of the reflection paper on the EU approach to collect and analyse PED should inform CAT secretariat.

### 7.3.2. Streamlining of BWP operations

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Scope: Discontinuation of systematic discussions of ATMP quality variations

**Action:** for discussion

CAT noted the proposal from BWP to discuss quality type II variations for ATMPs based on a risk-based approach. The criteria for selection of procedures for BWP discussion were presented.

## 7.4. Cooperation with the EU regulatory network

### 7.4.1. Support to member states for the assessment of ATMP Marketing Authorisation Applications

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CAT: Ilona Reischl

Scope: General discussion on needs and start of survey on resources (ATMP assessors) available in the NCAs

**Action:** for discussion

This topic will be discussed in an ad-hoc CAT meeting on 19.09.2023.

## 7.5. Cooperation with international regulators

### 7.5.1. ATMP cluster teleconference with US-FDA, Health Canada and PMDA (Japan)

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CAT: Ilona Reischl

Scope: Agenda of the teleconference that will take place on 28.09.2023

**Action:** for information

The agenda topics proposed by FDA and Health Canada were presented and agreed. The remaining CAT topic from the previous ATMP cluster meeting will be postponed due to unavailability of the CAT Rapporteur.

### 7.5.2. WHO considerations in developing a regulatory framework for human cells and tissues and for advanced therapy medicinal products

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CAT: Ilona Reischl

Scope: Final Considerations document (adopted March 2023)

**Action:** for information

The information was noted.

### 7.5.3. International Pharmaceutical Regulatory Programme (IPRP): Gene therapy and Cell therapy working groups

---

CAT: Pille Säälük

Scope: Merger of the gene therapy and cell therapy working groups

**Action:** for information

The information on the merger of the gene therapy and cell therapy working groups was noted. CAT was also informed that Ivana Haunerova is standing down as CAT representative for the cell therapy working group. Pille Säälük confirmed that she will continue as CAT representative for the (joined) IPRP gene and cell therapy working group.

## 7.6. CAT work plan

### 7.6.1. CAT work plan for 2024

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CAT: Ilona Reischl

Scope: First reflection on work plan topics for 2024

**Action:** for discussion

CAT discussed the activities from the work plan for 2023 and identified those that are likely to be included in the CAT work plan for 2024. Additional work plan topics were discussed (including those linked to the 15-year anniversary).

## 7.6.2. CAT Stakeholder meeting of 16 May 2023

---

CAT: Ilona Reischl

Scope: Draft minutes of the CAT stakeholder meeting

**Action:** for adoption

The minutes of the CAT stakeholder meeting were adopted.

## 7.7. Planning and reporting

### 7.7.1. Business Pipeline Report

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Scope: Q3/2023 Update of the Business Pipeline report for the human scientific committees

**Action:** for information

The information was noted.

## 7.8. Others

### 7.8.1. FDA Public workshop: Assessing genetic heterogeneity in the context of genome editing off-targets in gene therapy products

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CAT: Ilona Reischl

Scope: Summary of the FDA public workshop that was held on 16 December 2022

**Action:** for information

The information was noted.

### 7.8.2. CASSS China – 3<sup>rd</sup> CMC Strategy Forum for Biological Products (12-13 October 2023)

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CAT: Ilona Reischl

Scope: Request for a speaker

**Action:** for information

CAT members interested to take part in the CASSS China strategic forum should inform the CAT Secretariat.

### 7.8.3. FDA Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products

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CAT: Ilona Reischl

Scope: Guidance of industry published on FDA website (August 2023)

**Action:** for information

The FDA considerations document was noted.

## 8. Any other business

No item

Date of next CAT meeting:

04-06 October 2023

## 9. List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 06-08 September 2023 meeting.

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Ilona Reischl	Chair	Austria	No interests declared	
Silke Dorner	Member	Austria	No interests declared	
Corina Spreitzer	Alternate	Austria	No restrictions applicable to this meeting	
Claire Beuneu	Member	Belgium	No interests declared	
Olga Kholmanskikh	Alternate	Belgium	No interests declared	
Rozalina Kulaksazova	Member	Bulgaria	No interests declared	
Azra Selimovic	Member	Croatia	No interests declared	
Rafaella Pontou	Member	Cyprus	No interests declared	
Isavella Kyriakidou	Alternate	Cyprus	No interests declared	
Petr Soukup	Member	Czechia	No interests declared	
Kristyna Rehorova Hradilkova	Alternate	Czechia	No interests declared	
Ebru Karakoc Madsen	Member	Denmark	No interests declared	
Bibi Fatima Syed Shah	Alternate	Denmark	No interests declared	
Toivo Maimets	Member	Estonia	No interests declared	
Pille Saalik	Alternate	Estonia	No interests declared	

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Heli Suila	Member	Finland	No interests declared	
Violaine Closson Carella	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Jan Mueller-Berghaus	Member (CHMP co-opted member)	Germany	No interests declared	
Egbert Flory	Alternate (to CHMP representative)	Germany	No interests declared	
Maria Gazouli	Member	Greece	No interests declared	
Angeliki Rompoti	Alternate	Greece	No restrictions applicable to this meeting	
Maura O'Donovan	Member	Ireland	No interests declared	
Niamh Curran	Alternate	Ireland	No interests declared	
Concetta Quintarelli	Member	Italy	No interests declared	
Barbara Bonamassa	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Nancy De Bremaeker	Member	Luxembourg	No interests declared	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Johannes Hendrikus Ovelgonne	Member	Netherlands	No interests declared	
Dariusz Sladowski	Member	Poland	No restrictions applicable to this meeting	
Maria Isabel Borba Vieira	Alternate (to CHMP representative)	Portugal	No interests declared	
Silviu Istrate	Member	Romania	No interests declared	
Katarina Vavrová	Member	Slovakia	No interests declared	
Margareta Fogelová	Alternate	Slovakia	No interests declared	
Metoda Lipnik-Stangelj	Member	Slovenia	No interests declared	

<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Suzana Vidic	Alternate	Slovenia	No participation in final deliberations and voting on:	2.11.9 Kymriah II/72 2.11.12 Zolgensma II/40 2.13.2 Kymriah LEG/021
Sol Ruiz	Member (CHMP co-opted member)	Spain	No interests declared	
Marcos Timón	Alternate (to CHMP representative)	Spain	No interests declared	
Maria Luttgen	Member	Sweden	No restrictions applicable to this meeting	
Charlotte Anderberg	Alternate	Sweden	No interests declared	
Alessandra Renieri	Alternate	Clinicians' Representative	No restrictions applicable to this meeting	
Kerstin Sollerbrant Melefors	Member	Patients' Representative	No interests declared	
Mencia de Lemus Belmonte	Alternate	Patients' Representative	No restrictions applicable to this meeting	
Kieran Breen	Member (Vice-Chair)	Patients' Representative	No interests declared	
Catherine Milne	Observer/Alternate	EDQM	No interests declared	
Torbjorn Callreus	Expert	Malta	No interests declared	
Brigitte Müller	Expert	Austria	No interests declared	
Philipp Janesch	Expert	Austria	No interests declared	
Hanna Kankkonen	Expert	Finland	No interests declared	
Tia Hirvonen	Expert	Finland	No interests declared	
Paula Grönroos	Expert	Finland	No interests declared	
Karri Penttilä	Expert	Finland	No interests declared	
Johanna Lähteenvuo	Expert	Finland	No interests declared	
Martina Schübler-Lenz	Expert	Germany	No interests declared	
Beate Mosl	Expert	Germany	No interests declared	
Juliane Rau	Expert	Germany	No interests declared	



<u>Name</u>	<u>Role</u>	<u>Member State or affiliation</u>	<u>Outcome restriction following evaluation of e-DoI</u>	<u>Topics on agenda for which restrictions apply</u>
Attila Sebe	Expert	Germany	No interests declared	
Odoardo Olimpieri	Expert	Italy	No interests declared	
Antonella Isgrò	Expert	Italy	No interests declared	
Federico De Angelis	Expert	Italy	No interests declared	
Sean Barry	Expert	Ireland	No restrictions applicable to this meeting	
Silke Schüle	Expert	Germany	No interests declared	
Denise Tischner	Expert	Germany	No restrictions applicable to this meeting	
Boje Kvorning Pires Ehmsen	Expert	Denmark	No interests declared	
Torsten Holm Nielsen	Expert	Denmark	No interests declared	
Carolina Prieto	Expert	Spain	No interests declared	
Macarena Gajardo	Expert	Spain	No interests declared	
Katrin Féchir	Expert	Germany	No interests declared	
Silvia Vogl	Expert	Germany	No interests declared	
Johanna Reul	Expert	Germany	No interests declared	
Gaëlle De Meyer	Expert	Belgium	No restrictions applicable to this meeting	
Meeting run with support from relevant EMA staff				

## 10. Explanatory notes

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

For a list of acronyms and abbreviations, see:

[List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in relation to EMA's regulatory activities](#)

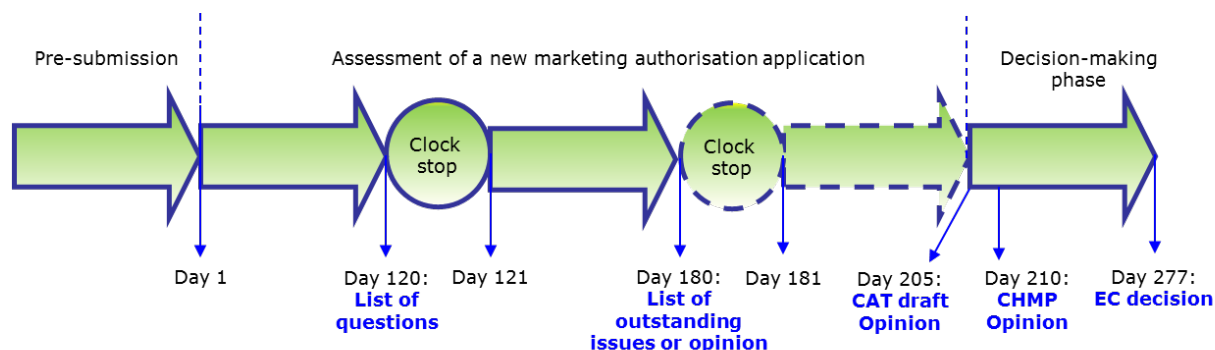
### Evaluation of ATMPs (section 2)

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 Post-authorisation activities (section 2.11-2.13) and any ATMP related inspection requests (section 2.14).

#### *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 2.4) 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 2.3)). Section 2.6 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.

#### *New applications (section 2.7.)*

In this section, information is included on upcoming marketing authorisation applications for ATMPs, as well as information on appointment of Rapporteurs for new ATMP applications.

### *Withdrawal of applications (section 2.8.)*

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.

### *Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.9.)*

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.

### *Companion diagnostics (section 2.10)*

This section lists applications for initial and follow-on consultation of companion diagnostics.

### *Post-authorisation activities (section 2.11-2.13.)*

Section 2.11 lists type II variations, including extension of indication applications and re-examination procedures for type II variations for which the applicant has requested re-examination of the opinion previously issued by the CHMP. Section 2.12 list extension application according to Annex I of Reg. 1234/2008 and section 2.13 includes all other post-authorisation activities concerning authorised ATMPs that are not covered elsewhere in the agenda such as post-authorisation measures, 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.

### *GMP and GCP Inspections Issues (section 2.14.)*

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).

## **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](#).

#### *Priority Medicines (PRIME)*

This section includes the new requests for eligibility to PRIME for ATMPs under development, the discussions in CAT of these eligibility requests and the final recommendations for eligibility of ATMPs adopted by CHMP.

CAT will appoint one of its members as the CAT sponsor for each new ATMP eligibility request who will lead the CAT discussion based on the recommendation from the SAWP.

### **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/)