17 March 2021
EMA/CAT/250178/2021
Human Medicines Division

# Committee for Advanced Therapies (CAT)

## Minutes of the meeting on 17-19 February 2021

Chair: Martina Schüßler-Lenz; Vice-Chair: Ilona Reischl

**Disclaimers**

Some of the information contained in these minutes are considered commercially confidential or sensitive and therefore not disclosed. Regarding 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. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), 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 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. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

The CAT chair welcomed Silviu Istrate and Alexandrina Preda, the new member and alternate for Romania.

## 1.2. Adoption of agenda

The CAT agenda for 17-19 February 2021 meeting was adopted.

## 1.3. Adoption of the minutes

The CAT minutes for 20-22 January 2021 meeting 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. Idecabtagene vicleucel - Orphan - EMEA/H/C/004662

Celgene Europe BV; treatment of multiple myeloma

Scope: List of Outstanding Issues

**Action:** for adoption

List of Outstanding Issues adopted on 04.12.2020. List of Questions adopted on 11.09.2020.

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

CAT adopted the second list of outstanding questions.

## 2.4. Day 120 list of questions

### 2.4.1. Lenadogene nolparvovec - Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber Hereditary Optic Neuropathy (LHON)

Scope: Day 120 list of questions

**Action:** for adoption

The Rapporteurs presented the assessment of the marketing authorisation application.

The list of questions was adopted, together with the response timetable.

## 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. GMP and GCP inspections requests

No items

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

### 2.11.1. Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0041/G

Amgen Europe B.V.

Rapporteur: Olli Tenhunen

Scope: Quality. Opinion

**Action:** for adoption

The opinion was adopted.

### 2.11.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0030

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Clinical
Update of section 5.1 of the SmPC to include the complete data set (updated overall survival analysis) of study CCTL019B2205J, a Phase II, single arm, multicenter study to determine the efficacy and safety of Kymriah in paediatric subjects with relapsed or refractory B-cell Acute lymphoblastic leukaemia (ALL). The clinical results have already been assessed in procedure EMA/H/C/004090/P46/011.
In addition, the final ATC code for tisagenlecleucel (L01XX71) has been added as an editorial change.

**Action:** for adoption

Request for Supplementary Information adopted on 22.01.2021.

See also 2.13.1., 2.13.2., 2.13.3

The opinion was adopted.

### 2.11.3. Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0021/G

CO.DON AG

Rapporteur: Lisbeth Barkholt

Scope: Quality

Request for supplementary information (RSI)

**Action:** for adoption

The RSI was adopted.

### 2.11.4. Yescarta - axicabtagene ciloleucel - Orphan - EMEA/H/C/004480/II/0028

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kristine Stark

Scope: Clinical. 2nd Request for Information
To update SmPC sections; 4.4 on Cytokine release syndrome (CRS) grading and neurologic adverse reactions; 4.8 on safety profile summary; 5.1 on follow up analysis; to update the safety information based on updates from study KTE-C19-101, entitled "A Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-C19 in Subjects with Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1)", the pivotal study for Yescarta. The updates

include the Phase 2 safety management ZUMA-1 Cohort 4, which was intended to assess the impact of earlier interventions (tocilizumab and/or corticosteroids, in addition to prophylactic levetiracetam) on the rate and severity of CRS and neurologic events; and data from a 36-month analysis from ZUMA-1 Cohorts 1 and 2.
The updated RMP version 3.1 has also been submitted.

**Action:** for adoption

Request for Supplementary Information (RSI) adopted on 09.10.2020.

The Rapporteur presented the outcome of the assessment of the responses to the RSI. A second RSI was adopted.

### 2.11.5. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0008

Novartis Gene Therapies EU Limited

Rapporteur: Carla Herberts

Scope: Safety
Updates to SmPC sections 4.2, 4.4 and 4.8 to reflect the risk of Thrombotic Microangiopathy, recommend additional tests to help early identification of this risk and advice for prompt clinical management.
The Package Leaflet is updated accordingly.

**Action:** for adoption

Request for Supplementary Information adopted on 04.12.2020.

The Rapporteur presented the outcome of the assessment, the advice from PRAC to CAT and the Dear Health Care Professional (DHPC) letter. The changes to the SmPC were discussed. The opinion and DHCP letter were adopted.

## 2.12. Extension applications

No items

## 2.13. Other Post-Authorisation Activities

### 2.13.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/003.4

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: PhV
Study: CCTL019B2401
Non-interventional post-authorisation safety study (PASS): In order to further characterise the safety – including long-term safety – of Kymriah, the applicant should conduct and submit a study based on data from a disease registry in ALL and DLBCL patients.
***Annual safety reports and 5-yearly interim reports***

**Action:** for adoption

See also 2.11.2., 2.13.2., 2.13.3.

CAT adopted the Rapporteurs assessment report.

### 2.13.2. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/ANX/008.1

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: PhV
***Interim Clinical study report*** / study CCTL019C2201 (24 months follow-up for all infused patients in the main Cohort)
Addressing partially the Annex II PAES ANX008:
"In order to further characterise the long term efficacy and safety of Kymriah in relapsed/refractory diffuse large B-cell lymphoma (DLBCL), the applicant should submit the 24 months follow up of all infused patients from study C2201. In addition, the applicant should submit the final CSR including 5 years of follow up".

**Action:** for adoption

See also 2.11.2., 2.13.1., 2.13.3.

CAT adopted the Rapporteurs assessment report.

### 2.13.3. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/MEA/005

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: Pharmacovigilance.
From Initial MAA: Study CCTL019A2205B: Long-term follow-up of patients exposed to lentiviral-based CD19 directed CAR-T-cell therapy. The primary objective is to describe selected, delayed AEs suspected to be related to previous CD19 CAR-T-cell therapy as outlined in current Health Authority guidelines. The secondary objectives are to monitor the persistence of CD19 CAR transgene in peripheral blood, monitor the expression of replication competent lentiviruses, assess the long-term efficacy of CD19 CAR-T, monitor lymphocyte levels and describe the growth, development, and female reproductive status for patients who were aged <18 years at the time of the initial CD19 CAR-T-cell infusion. (Category 3).

**Action:** for adoption

See also 2.11.2., 2.13.1., 2.13.2

CAT adopted the Rapporteurs assessment report.

### 2.13.4. Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence - Orphan - EMEA/H/C/003854/R/0029

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruiz, Co-Rapporteur: Egbert Flory, PRAC Rapporteur: Menno van der Elst

Scope: 5-year Renewal of Marketing Authorisation

**Action:** for adoption

Request for Supplementary Information adopted on 04.12.2020.

The CAT Rapporteur presented the outcome of the assessment of the responses to the RSI. CAT discussed one leukaemia case following an insertional mutagenesis event and the changes to the product information and RMP linked to this safety finding. The CAT agreed with the Rapporteur's conclusion that the benefit / risk profile of Strimvelis remains positive. The feedback from the PRAC and the DHPC letter was noted. CAT proposed to have a second renewal for the MA.

The renewal opinion and the DHCP letter were adopted.

### 2.13.5. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/C/003691/R/0018

Bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson-Carella, PRAC Rapporteur:

Brigitte Keller-Stanislawski

Scope: 1-year Renewal of Marketing Authorisation. Opinion

**Action:** for adoption

Request for Supplementary Information adopted on 22.01.2021.

The Rapporteur presented the information provided by the MAH on a case of Acute Myeloid Leukaemia (AML) in a patient with sickle cell disease treated with the investigational product bb1111. As this product uses the same lentiviral vector to transduce the cell as for Zynteglo, the MAH put the marketing of Zynteglo as well as all trial with bb1111 on hold. Investigations are ongoing to determine if the AML is caused by an insertional mutagenesis event by the lentiviral vector.

Further to this information, CAT discussed the regulatory considerations. The Rapporteur's view to discuss this safety finding outside of the renewal procedure was agreed. An article 20 referral procedure was initiated by the Commission, asking EMA to confirm the benefit risk profile of Zynteglo in the light of the new safety finding: PRAC and CAT will be involved in this referral.

The renewal procedure has been put on hold pending the finalisation of the referral procedure.

### 2.13.6. Options paper on using the European Society for Blood & Marrow Transplantation (EBMT) as a data source for long-term safety and efficacy follow-up of EU patients receiving ATMPs

Scope: summary of MS responses; recommendation for way forward

**Action:** for discussion

The feedback from the member states on the EMA options paper was presented. Different approaches were proposed for marketed products and new products. Both approaches will now be further developed. Further feedback will be provided at the next CAT meeting.

## 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: | 19.02.2021 |
| -Draft EMA Co-ordinator's report: | 02.03.2021 |
| -CAT Coordinator's comments: | 10.03.2021 |

-Revised scientific recommendation: 12.03.2021
-Discussion of scientific recommendation by CAT: 19.03.2021

## 4.1. New requests – Appointment of ITF Coordinator

### 4.1.1. Autologous antigen specific Cytotoxic T Lymphocytes

Intended for the treatment of cancer patients that are over expressing the specific antigen

Scope: appointment of CAT Coordinator and adoption of timetable

**Action:** for adoption

The CAT coordinator was appointed.

### 4.1.2. Autologous dendritic cells activated against tumour peptides

Intended for the treatment of cancer patients; *in vivo* immune stimulation against specific cancer overexpressing the tumour antigen

Scope: appointment of CAT Coordinator and adoption of timetable

**Action:** for adoption

The CAT coordinator was appointed.

### 4.1.3. Autologous M1-polarized macrophages

Intended for the treatment of cancer patients

Scope: appointment of CAT Coordinator and adoption of timetable

**Action:** for adoption

The CAT coordinator was appointed.

### 4.1.4. Autologous Cytotoxic Natural Killer (NK) cells

Intended for the treatment of cancer patients

Scope: appointment of CAT Coordinator and adoption of timetable

**Action:** for adoption

The CAT coordinator was appointed.

### 4.1.5. Autologous plasma cells producing monoclonal antibodies against specific tumor antigen, for treatment of cancer patients

Intended for the treatment of cancer patients

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 human mesenchymal stem cells derived from Wharton's jelly, muscle and tendons disease

Intended for diseases of muscles and tendons

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.2. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, anal fistula

Intended for the treatment of anal fistula

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.3. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, androgenic alopecia

Intended for the treatment of androgenic alopecia, unspecified

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.4. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, diabetic foot syndrome

Intended for the treatment of diabetic foot syndrome (DFS)

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.5. Allogeneic human mesenchymal stem cells derived from Wharton's jelly, Parkinson's disease

Intended for the treatment of Parkinson's disease

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.6. Allogeneic human mesenchymal stem cells derived from Whartons jelly seeded on the dermal scaffold, skin ulcers

Intended for the treatment of skin ulcers

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.7. Autologous human mesenchymal stem cells derived from adipose tissue, anal fistula

Intended for the treatment of anal fistula

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.8. Autologous human mesenchymal stem cells derived from adipose tissue, androgenic alopecia

Intended for the treatment of androgenic alopecia, unspecified

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.9. Autologous human mesenchymal stem cells derived from adipose tissue, muscle and tendons disease

Intended for diseases of muscles and tendons

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.10. Two mRNA active substances, encoding separately for Human Papilloma Virus type (HPV) 16 E6 and HPV16 E7 protein

Intended for the treatment of recurrent/metastatic HPV16-positive carcinoma

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.11. Human amniotic membrane, allogeneic, sterile, cryomilled and lyophilized

Intended for the treatment of symptoms of osteoarthritis

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.12. Autologous dendritic cells activated against SARS-COV-2 peptides

Intended for the prevention of SARS-COV-2 infection

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. AT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.13. Human umbilical cord MSC derived exosomes carrying recombinant hTERT mRNA and protein, hsa-miR-125b-5p, hsa-miR-125b-1-3p, AntimiR-21-5p

Intended for the treatment of Acute Respiratory Distress Syndrome and Chronic Obstructive Respiratory Disease

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.14. DNA plasmid encoding human transferring gene

Intended for the treatment of retinitis pigmentosa

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

### 4.2.15. Bacteriophage cocktail consisting of four CRISPR-armed phages

Intended for the treatment of prophylaxis of bloodstream E. coli infection in neutropenic patients with haematological malignancy

Scope: ATMP scientific recommendation

**Action:** for adoption

CAT discussed the ATMP classification report. CAT secretariat to send the draft scientific recommendation to the European Commission for comments by 5 March 2021.

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

No items

## 4.4. Finalisation of procedure

### 4.4.1. Autologous bone marrow aspirate concentrate

Intended for the repair mechanism for bone repair in a variety of bony defects such as fractures, arthroplasty, bone cysts, osteonecrosis, or avascular necrosis

Scope: the European Commission has raised no comments. ATMP scientific recommendation

**Action:** for information

The information was noted. The classification report will be sent to the applicant.

### 4.4.2. *In vitro* expanded autologous human articular chondrocytes

Intended for the repair of symptomatic, localised, full-thickness cartilage defects of the knee joint in patients with closed epiphyseal growth plates.

Scope: comments from the European Commission. Revised ATMP scientific recommendation

**Action:** for adoption

The revised report was adopted. The classification report will be sent to the applicant.

## 4.5. Follow-up and guidance

No items

# 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

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

Timetable:

| | |
|---|---|
| -Start of procedure at SAWP: | 08/02/2021 |
| -Appointment of CAT Peer Reviewers: | 19/02/2021 |
| -SAWP first reports: | 01/03/2021 |
| -CAT Peer reviewer comments: | 05/03/2021 |
| -Discussion at SAWP: | 08-11/03/2021 |
| -Discussions at CAT and feedback to SAWP: | 19/03/2021 |

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

Timetable:

| | |
|---|---|
| -Start of procedure at SAWP: | 11/03/2021 |
| -Appointment of CAT Peer Reviewers: | 19/03/2021 |
| -SAWP First Reports: | 29/03/2021 |
| -CAT Peer reviewer comments: | 02/04/2021 |
| -Discussion at SAWP: | 09/04/2021 |
| -Discussions at CAT and feedback to SAWP: | 16/04/2021 |

## 5.2. CAT discussion

## 5.3. List of Issues

## 5.4. Finalisation of SA procedures

# 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

Timetable for assessment:

| | |
|---|---|
| Procedure start: | 11.02.2021 |
| SAWP recommendation: | 11.03.2021 |
| CAT recommendation: | 19.03.2021 |
| CHMP adoption of report and final recommendation: | 25.02.2021 |

### 6.3.2. Month 1 – Discussion of eligibility

### 6.3.3. Month 2 – Recommendation of eligibility

### 6.3.4. Ongoing support

# 7. Organisational, regulatory and methodological matters

## 7.1. Mandate and organisation of the CAT

### 7.1.1. CAT membership

Romania – Silviu Istrate – membership mandate (member) started on 12 February 2021
Romania – Alexandria Preda – membership mandate (alternate) started on 12 February 2021

**Action:** for information

The CAT chair welcomed the new members.

### 7.1.2. Strategic Review & Learning meeting (SRLM) under the Portuguese presidency of the European Union - Lisbon, Portugal

CAT: Bruno Sepodes, Maria-Isabel Vieira

Scope: topics for the agenda of the SRLM meeting, to take place on 27th May 2021

**Action:** for discussion

The agenda topics proposed by the Portuguese members were discussed. The proposed speaker will be asked to provide some more information on the content of their talks. It was proposed to include one addition talk on the use of ATMPs in Portugal. The updated agenda will be presented at the next CAT.

## 7.2. Coordination with EMA Scientific Committees

No items

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

### 7.3.1. Re-engineered Innovation Task Force (ITF)

Scope: awareness of the re-engineered informal discussion platform on novel technologies, methods and substances including EU network (including feedback on 2020 activities with focus on ATMPs). Discussion on best way to interact / involve CAT members in respective relevant meetings on innovative technologies and developments.

**Action:** for discussion

Note: this is a follow-up from interviews Jordi Llinares García held with Committee chairs and a consequent discussion SciCoBo meeting that took place in December 2020.

CAT noted the presentation on the collaboration between CAT and the re-engineered ITF, and the possibility for CAT members to be involved in non-ATMP specific topics (e.g. discussions on decentralised trials, GMP). Feedback from CAT was also sought on most relevant developments from 2020. The Commission representation mentioned the need to make a link with the Commission initiative 'Pharmaceutical strategy for Europe': some of the work packages relate to innovation and how this challenges the current legal framework.

### 7.3.2. New scientific advice (SA) procedure for ATMPs

Scope: template for CAT Peer Reviewer's comments on the SA first reports

**Action:** for discussion

The new SA procedure is starting this month: the CAT peer reviewers will provide comments on the first reports by the SAWP Rapporteur. The template for comments was presented, and further guidance was provided on the new interactions between CAT and SAWP. The template will be a living document: it will capture the comments from the CAT peer reviewer, feedback from the SAWP discussion, any specific comments from SAWP to CAT and a summary of the CAT discussion. Further to the discussion, refinements will be made to the template. The template will thereafter be included in CAT MMD/General/Templates.
CAT agreed to implement the new SA procedure and try out the proposed template: a review of the procedure will take place in 6 months time.

### 7.3.3. EMA draft pregnancy strategy

Scope: update on what is done to further develop and implement the strategy and to obtain feedback on committee needs in this area.

**Action:** for discussion

Note: since July 2020 EMA has started the international collaboration on building an infrastructure for drug safety in pregnancy studies (building on the work initiated for COVID & pregnancy), held a stakeholders workshop and published the report from this (available at https://www.ema.europa.eu/en/documents/report/report-workshop-benefit-risk-medicines-used-during-pregnancy-breastfeeding_en.pdf).

A presentation was made to CAT on the EMA pregnancy strategy, for their awareness and comments. CAT members mentioned that the guideline from the Clinical Trial Facilitation Group on Pregnancy makes it difficult to include women on child bearing potential and pregnant women in clinical trials, resulting in very limited clinical trial data being generated in pregnancy. As a result, and as described in the CHMP guideline on labelling recommendation for the SmPC, this result is very restrictive/defensive statement in the SmPC related to use of the medicine during pregnancy / lactation. There was a question to include information (on the EMA website) on the use of Covid-19 vaccines during pregnancy.

### 7.3.4. Working Party with Patients' and Consumers' Organisations (PCWP) and Working Party with Healthcare Professionals' Organisations (HCPWP)

Scope: draft agenda for the PCWP/HCPWP joint meeting, 3-4 March 2021

**Action:** for information

Note: the CAT Chair - Martina Schüßler-Lenz - will take part on the topic of: *'Timely patients'* access to advanced therapy medicinal products in the EU'

The information was noted.

## 7.4. Cooperation within the EU regulatory network

### 7.4.1. Revision of the EU legislation on blood, tissues and cells (BTC)

CAT: Ilona Reischl

Scope: CAT's input to the public consultation on the revision of the BTC legislation

**Action:** for discussion

Note: the online **public consultation** on the BTC is opened on the 'Have Your Say' portal of the European Commission. Submissions will be accepted up to 15 April 2021. In parallel to the public consultation, a **targeted consultation** has also been launched with the same closing date. This consultation is targeting organisations that are directly involved in, or impacted by, the BTC legislation and that are familiar with the legal framework. Those organisations are invited to complete both consultations, starting with the public consultation and then proceeding to complete the targeted one. You can follow the full revision process on our DG SANTE web-page.

CAT members were asked to contribute to the targeted consultation.

CAT noted the Registration of interest to take part in BTC Impact Assessment Workshops: CAT involvement is only mentioned in one of the workshops (Borderline with other regulated frameworks: classification advice and interplay); CAT involvement in other workshops might also be relevant, e.g. on Regulation Point-of-Care BTC processing.

Further feedback will be provided to CAT's involvement in specific meetings, workshops and interview organised by the European Commission, DG Santé (see minutes of the December 2020 CAT meeting, topic 7.4.2).

### 7.4.2. European Commission's Q&A on orphan similarity assessment for ATMPs

Scope: Proposal to update of the Commission's Q&A related to the assessment of similarity for ATMPs in the context of the orphan legislation, in line with the experience gained

**Action:** for discussion

Note**:** published Q&A:
https://ec.europa.eu/health/sites/health/files/files/orphanmp/doc/2018_qa_atmps_en.pdf

The Commission Representative presented the aim of the revision of the Q&A on orphan similarity.

Because of the link with the New Active Substance (NAS) status, the colleagues involved in that workplan topic (see 7.6.1) will contribute to this revision. The following additional CAT members will join: Claire Beuneu, Rune Kjeken, Violaine Closson-Carella.

The Commission will organise some teleconference meetings with the drafting group and report back to CAT when an updated draft Q&A has been developed.

## 7.5. Cooperation with international regulators

### 7.5.1. Definition of gene therapy medicinal products

CAT ad-hoc drafting group: Belaïd Sekkali, Egbert Flory, Marcos Timón Violaine Closson Carella, Ilona Reischl, Toivo Maimets, Rune Kjeken, Claire Beuneu, Rocío Salvador Roldán.

Scope: ad-hoc drafting group's report on the comparison of the ICH vs. EU definitions of GTMPs

**Action:** for adoption

Note: during the drafting of the ICH S12 guideline, a definition of a gene therapy products has been included. On request of the European Commission (letter of 11 December 2010), CAT compared the ICH and EU GTMP definitions and reflected on the adequacy of the ICH definition.

The outcome of the comparison of the gene therapy definitions in the ICH S12 guideline and the EU legislation was presented. Further to the discussion, some clarification was proposed to the statement on synthetic nucleotides. The report was adopted with this amendment and will be sent to the Commission.

The Ad-hoc drafting group will now continue reflecting on how to update the EU-GTMP definition, to bring it in line with progress in science (e.g. on genome editing tools).

At the March meeting, detailed feedback will be provided on the progress of the drafting of the ICH-S12 guideline.

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

CAT: Martina Schüssler-Lenz

Scope: draft agenda of the teleconference to take place on 25 February 2021

**Action:** for discussion

CAT was informed that this ATMP cluster teleconference will not take place. The next ATMP cluster TC is scheduled to take place on 25 March 2021.

## 7.6. CAT work plan

### 7.6.1. CAT work plan

CAT: Martina Schüßler-Lenz

Scope: workplan topic on use of real-world data in regulatory decision making of ATMPs

**Action:** for discussion

Further to a question (e-mail) from the CAT chair, members were asked if they could join the topic on the use of real-world data. It was agreed that additional experts from the assessment teams of ATMPs will contribute to this activity.

For the workplan topic on New Active Substance, Barbara Bonamassa (expert from Italy) will be added to the list of contributors.

With these two additions, the CAT workplan will now be published.

## 7.7. Planning and reporting

No items

## 7.8. Others

### 7.8.1. Scientific talk: Mesenchymal stem cells

CAT: Martina Schüßler-Lenz

Scope: Presentation by: Attila Sebe, M.D., clinical assessor, Abteilung Medizinische Biotechnologie, Paul-Ehrlich-Institut

**Action:** for information

CAT noted the presentation by Attila Sebe on the uncertainties associated with the definition of what are mesenchymal stem cells and mechanism of action of these cells.

### 7.8.2. Curriculum on Advanced Therapies Medicinal Products (ATMPs)

CAT: Ilona Reischl

Scope: plan of trainings for 2021

**Action:** for discussion

Topic postponed until the March CAT meeting

# 8. Any other business

### 8.1. Process for documenting of CAT experiences / CAT learning

CAT: Martina Schüssler Lenz, Niamh Curran, Carla Herberts, Heli Suila

Scope: review of the CAT learnings and presentation of learnings

**Action:** for agreement

The key learnings were discussed, and amendments were introduced. The learnings were agreed. The document will be updated and included in CAT MMD/General/CAT learnings.

## 8.2. Participation of CAT members/alternates as speakers or panellist to international conferences

Scope: CAT participation to the International Society for Stem Cell Research (ISSCR) Workshop on clinical translation

**Action**: for discussion

Note: the CAT chair and vice chair received invitations to give a presentation at the 2021 ISSCR Workshop on Clinical Translation: Translating iPS Cell-based Therapies to the Clinic (7 June 2021)

No CAT representative was identified for this presentation.

Date of next CAT meeting:

17-19 March 2021

# 9. Explanatory notes

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

### Abbreviations / Acronyms

AAV: Adeno-Associated Virus

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

CTFG: Clinical Trial Facilitation Group

DG: Drafting Group

EC: European Commission

EU NTC: European Union Network Training Centre

ERA: Environmental Risk Assessment

FDA: Food and Drug Administration

FL: Final Letter

GCG: Guideline Consistency Group

GCP: Good Clinical Practice

GLP: Good Laboratory Practice

GMO: Genetically-modified organism

GMP: Good Manufacturing Practice

GTMP: Gene Therapy Medicinal Product

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 Application

MAH: Marketing Authorisation Holder

MNAT: Multinational assessment team

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

QRD: Quality review of documents

RMP: Risk Management Plan

RP: Reflection paper

RSI: Request for supplementary information

SAs: Scientific Advices

SAG-O: Scientific Advisory Group Oncology

SAWP: Scientific Advice Working Party

SR: Summary Report

SWP: Safety Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

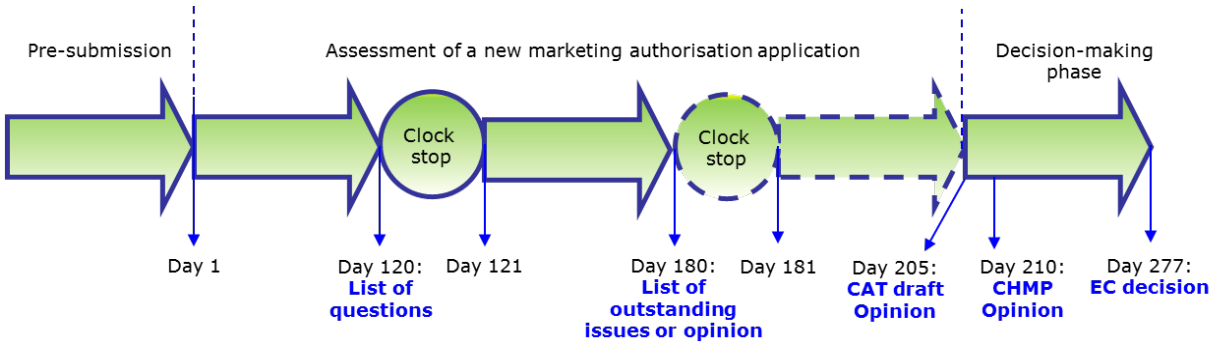
## Evaluation of ATMPs (section 2)

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.

*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/

## 10. List of participants

including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 17-19 February 2021 meeting.

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Martina Schüssler-Lenz | Chair | Germany | No interests declared | |
| Ilona Reischl | Member (Vice-Chair) | Austria | No interests declared | |
| Silke Dorner | Alternate | Austria | No interests declared | |
| Claire Beuneu | Member | Belgium | No interests declared | |
| Belaïd Sekkali | Alternate | Belgium | No interests declared | |
| Rozalina Kulaksazova | Member | Bulgaria | No interests declared | |
| Petra Sokol | Alternate | Croatia | No interests declared | |
| Rafaella Pontou | Member | Cyprus | No interests declared | |
| Ivana Haunerova | Member | Czechia | No interests declared | |
| Tomas Boran | Alternate | Czechia | No interests declared | |
| Anne Pastoft | Member | Denmark | No interests declared | |
| Toivo Maimets | Member | Estonia | No interests declared | |
| Pille Saalik | Alternate | Estonia | No interests declared | |
| Heli Suila | Member | Finland | No interests declared | |
| Violaine Closson | Member | 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 | |
| Katalin Lengyel | Member | Hungary | No interests declared | |
| Maura O'Donovan | Member | Ireland | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Niamh Curran | Alternate | Ireland | No restrictions applicable to this meeting | |
| Una Riekstina | Member | Latvia | No interests declared | |
| Liga Kunrade | Alternate | Latvia | No interests declared | |
| Raimondas Benetis | Alternate (to CHMP representative) | Lithuania | No interests declared | |
| Guy Berchem | Member | Luxembourg | No restrictions applicable to this meeting | |
| John J. Borg | Member (CHMP member) | | No interests declared | |
| Anthony Samuel | Alternate (to CHMP representative) | Malta | No interests declared | |
| Carla Herberts | Member | Netherlands | No interests declared | |
| Babs Fabriek | Alternate | Netherlands | No interests declared | |
| Rune Kjeken | Member | Norway | No restrictions applicable to this meeting | |
| Dariusz Śladowski | 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 | |
| Alexandrina Preda | Alternate | Romania | No interests declared | |
| Lukas Slovak | Member | Slovakia | No interests declared | |
| Alexandra Padova | Alternate | Slovakia | No interests declared | |
| 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 | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Lisbeth Barkholt | Member | Sweden | No interests declared | |
| Maria Luttgen | Alternate | Sweden | No restrictions applicable to this meeting | |
| Bernd Gänsbacher | Member | Healthcare Professionals' Representative | No interests declared | |
| Alessandro Aiuti | Member | Healthcare Professionals' Representative | Restrictions applicable to this meeting | |
| Kerstin Sollerbrant | Member | Patients' Representative | No interests declared | |
| Lydie Meheus | Alternate | Patients' Representative | No interests declared | |
| Kieran Breen | Member | Patients' Representative | No restrictions applicable to this meeting | |
| Roland Pochet | Alternate | Patients' Representative | No interests declared | |
| Conceptción Prieto Yerro | Expert - remotely | AEMPS.ES | No interests declared | |
| Macarena Rodriguez Mendizabal | Expert - remotely | AEMPS.ES | No interests declared | |
| Elena Morejón | Expert - remotely | AEMPS.ES | No restrictions applicable to this meeting | |
| Jesus Fominaya Guitierrez | Expert - remotely | AEMPS.ES | No interests declared | |
| Esther Rincón Gila | Expert - remotely | AEMPS.ES | No interests declared | |
| Andrea Laslop | Expert - remotely | AGES.AT | No interests declared | |
| Christoph Mueck | Expert - remotely | AGES.AT | No interests declared | |
| Mandred Schuster | Expert - remotely | AGES.AT | No restrictions applicable to this meeting | |
| Christine Vaculik | Expert - remotely | AGES.AT | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Angelina Doriguzzi | Expert - remotely | AGES.AT | No restrictions applicable to this meeting | |
| René Anour | Expert - remotely | AGES.AT | No interests declared | |
| Elisabeth Penninga | Expert - remotely | DKMA.DK | No interests declared | |
| Louise Frederikke Bang-Lauritsen | Expert - remotely | DKMA.DK | No interests declared | |
| Susanne Høpner Rasmussen | Expert - remotely | DKMA.DK | No restrictions applicable to this meeting | |
| Janneke (Johanna) van Leeuwen | Expert - remotely | CBG.MEB.NL | No interests declared | |
| Bjørg Bolstad | Expert - remotely | NOMA.NO | No interests declared | |
| Hilde Røshol | Expert - remotely | NOMA.NO | No interests declared | |
| Helga Haugon Olsen | Expert - remotely | NOMA.NO | No interests declared | |
| Fabrice Eroukhmann of | Expert - remotely | NOMA.NO | No restrictions applicable to this meeting | |
| Christian Gartner | Expert - remotely | AGES.AT | No restrictions applicable to this meeting | |
| Christian (Kit) Roes | Expert - remotely | Radboudumc.NL | No restrictions applicable to this meeting | |
| Attila Sebe | Expert - remotely | PEI-DE | No interests declared | |
| Barbara Bonamassa | Expert - remotely | AIFA.IT | No restrictions applicable to this meeting | |
| Odoardo Maria Olimpieri | Expert - remotely | AIFA.IT | No interests declared | |
| Michael Rosu-Myles | Obsever | Health Canada | | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| David Southam | Obsever | Health Canada | | |
| Donna Situ | Obsever | Health Canada | | |
| A representative from the European Commission attended the meeting<br>*For CMDh:* Ad hoc experts* and 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.