20 January 2021
EMA/CAT/162004/2021
Human Medicines Division

Committee for Advanced Therapies (CAT)

Minutes of the meeting on 02-04 December 2020

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

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 thanked Nathalie Morgensztejn and Hans Ovelgönne, whose mandate ended or is ending in November 2020 and December 2020 respectively, for their contributions to the CAT over the last years.

1.2. Adoption of agenda

The CAT agenda for 02-04 December 2020 meeting was adopted with one addition to 2.13 (Strimvelis).

1.3. Adoption of the minutes

The CAT minutes for 04-06 November 2020 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

Accelerated assessment

Celgene Europe BV; treatment of multiple myeloma

Scope: Day 180 List of outstanding issues

Action: for adoption

List of Questions adopted on 11.09.2020.

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

CAT agreed to switch from the accelerated review to a normal evaluation timetable.

2.4. Day 120 list of questions

No items

2.5. Day 80 assessment reports

2.5.1. Elivaldogene autotemcel - Orphan - EMEA/H/C/003690

Accelerated assessment

bluebird bio (Netherlands) B.V; treatment of patients less than 18 years of age with an *ABCD1* genetic mutation and early cerebral adrenoleukodystrophy

Scope: feedback on ongoing assessment

Action: for information

CAT noted the information.

2.6. Update on ongoing initial applications

No items

2.7. New applications

2.7.1. Lenadogene nolparvovec – Orphan - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of Leber Hereditary Optic Neuropathy

Scope: timetable for assessment

Action: for adoption

The timetable for assessment was adopted.

2.8. Withdrawal of initial marketing authorisation application

2.8.1. Artobend - autologous human chondrocytes in vitro expanded - EMEA/H/C/004598

Tetec Tissue Engineering Technologies AG; repair of cartilage defects of the knee joint

Scope: letter dated 19.11.20. from the applicant withdrawing the marketing authorisation application (MAA).

Action: for information

CAT noted the withdrawal of the marketing authorisation application for Artobend. Minimal information on the withdrawal will be published on the EMA website (a short question and answer and the withdrawal letter) as CAT has not yet adopted any assessment report (e.g. list of questions).

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 - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

2.11.1. Kymriah - tisagenlecleucel - Orphan - EMEA/H/C/004090/II/0027

Novartis Europharm Limited

Rapporteur: Rune Kjeken

Scope: Quality:

Action: for adoption

Request for Supplementary Information adopted on 06.11.2020, 09.10.2020.

The outcome of the assessment of the responses to the second request for supplementary information was presented. All issues are considered resolved. CAT noted the two recommendations taken by the company. The wording in SmPC introduced in the variation II/13 remains valid and will not be changed. The opinion was adopted.

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

Novartis Gene Therapies EU Limited

Rapporteur: Hans Ovelgönne

Scope: Clinical: Update to SmPC for sections 4.4 (Special warnings and precautions for use), 4.8 (Undesirable Effects) and corresponding sections in the Package Leaflet to add a new safety signal of 'Thrombotic microangiopathy'.

Action: for adoption

The Rapporteur presented the outcome of the assessment. Feedback was provided from the PRAC discussion on the new safety signal. A request for supplementary information was presented and adopted.

Depending on the responses, amendments to the SmPC will be discussed and the need for a 'Dear Healthcare Professional Communication' (DHPC) will be considered.

2.11.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/II/0009/G

Novartis Gene Therapies EU Limited

Rapporteur: Hans Ovelgönne

Scope: Quality

Action: for adoption

A request for supplementary information was adopted.

2.11.4. Zynteglo - betibeglogene autotemcel - Orphan - EMEA/H/C/003691/II/0017

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts

Scope: Quality

Action: for adoption

The opinion for this variation was adopted.

2.12. Extension applications

No items

2.13. Other Post-Authorisation Activities

2.13.1. 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 Ruíz

Scope: 5-year renewal, request for supplementary information.

Action: for discussion

See also 2.13.2

A list of questions was adopted.

2.13.2. 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

Orchard Therapeutics (Netherlands) BV

Rapporteur: Sol Ruíz; PRAC: Menno van der Elst

Scope: safety: report of a serious adverse event (lymphoid T cell leukaemia) potentially related to an insertional mutagenesis event

Action: for discussion

Information on the adverse event finding was reported. Feedback was also provided on the PRAC discussion on this topic. It was agreed to request additional information from the applicant . This information will be requested as part of the ongoing renewal application (see 2.13.1).

2.13.3. Zolgensma - onasemnogene abeparvovec - Orphan - EMEA/H/C/004750/REC/015

Novartis Gene Therapies EU Limited

Rapporteur: Hans Ovelgönne, CHMP Coordinator: Johann Lodewijk Hillege

Scope: from Letter of Recommendation

Action: for adoption

CAT agreed with the conclusion of the Rapporteur's report.

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:	21.12.2020
-Draft EMA coordinator's report:	08.01.2021
-CAT coordinator's comments:	13.01.2021
-Revised scientific recommendation:	15.01.2021
-Adoption of scientific recommendation by CAT:	22.01.2021

4.1. New requests – Appointment of CAT Coordinator

4.1.1. 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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Rapporteur was appointed.

4.1.2. *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: appointment of CAT Coordinator and adoption of timetable

Action: for adoption

The CAT Rapporteur was appointed.

4.2. Day 30 ATMP scientific recommendation

4.2.1. Autologous bone marrow derived mesenchymal stem cells (amyotrophic lateral sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

An ATMP classification was issued for this product in 2015. CAT considered that the change in the manufacture of the active substance will not change the outcome of the previous classification. Consequently, no new classification report has been issued.

4.2.2. Autologous bone marrow derived mesenchymal stem cells (multiple sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

An ATMP classification was issued for this product in 2018. CAT considered that the change in the manufacture of the active substance will not change the outcome of the previous classification. Consequently, no new classification report has been issued.

4.2.3. Autologous anti-CD19 chimeric antigen receptor T cells

Intended for the treatment of B- cell malignancies

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 18 December 2020.

4.2.4. Autologous omental adipose tissue and biodegradable fibrin glue

Intended for the treatment of renal traumatic/disease conditions

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 18 December 2020.

4.2.5. Messenger ribonucleic acid (mRNA) encoding the human glucose debranching enzyme (GDE)

Intended for the treatment of glycogen storage disease III

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 18 December 2020.

4.2.6. *In vitro* transcribed messenger ribonucleic acid (mRNA) encoding human interleukin 2 (IL-2), linked to interfering RNA targeting vascular endothelial growth factor A (VEGF-A)

Intended for the treatment of solid tumours

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 18 December 2020.

4.2.7. Wharton's jelly derived mesenchymal stem cells (WJ-MSCs) (multiple sclerosis)

Intended for the treatment of multiple sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

An ATMP classification was issued for this product in 2018. CAT considered that the change in the manufacture of the active substance will not change the outcome of the previous classification. Consequently, no new classification report has been issued.

4.2.8. Wharton's jelly derived mesenchymal stem cells (WJ-MSCs) (amyotrophic lateral sclerosis)

Intended for the treatment of amyotrophic lateral sclerosis

Scope: letter to the applicant on request for ATMP classification.

Action: for information

An ATMP classification was issued for this product in 2015 and in 2020. CAT considered that the change in the manufacture of the active substance will not change the outcome of the previous classification. Consequently, no new classification report has been issued.

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

No items

4.4. Finalisation of procedure

4.4.1. Autologous CD34+ cells transduced with a lentiviral vector encoding human cystinosin

Intended for the treatment of cystinosis

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

Action: for information

The information was noted.

4.4.2. 3D bio-printed bionic pancreas composed of islets of Langerhans and non-viable printable porcine-derived matrix plus porcine–derived decellularised blood vessel – H0005801

Intended for the treatment of late-chronic pancreatitis

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

Action: for information

The information was noted.

4.4.3. 3D bio-printed bionic pancreas composed of insulin- and glucagon-releasing cells and non-viable printable porcine-derived matrix plus porcine–derived decellularised blood vessel – H0005802

Intended for the treatment of brittle diabetes mellitus type I

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

Action: for information

The information was noted.

4.4.4. Autologous tumour-infiltrating lymphocytes

Intended for the treatment of advance melanoma

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

Action: for information

The information was noted.

4.4.5. Delolimogene mupadenorepvec (oncolytic adenovirus expressing two immunostimulatory transgenes (TMZ-CD40L and 4-1BBL))

Intended for the treatment of cancer

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

Action: for information

The information was noted.

4.4.6. Allogeneic cord tissue-derived mesenchymal stromal cells

Intended for the treatment of inflammatory and immunological diseases (acute graft-versus-host disease, systemic lupus erythematosus, systemic sclerosis, acute respiratory distress syndrome)

Scope: the European Commission raised minor comments. ATMP scientific recommendation

Action: for information

The information was noted.

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 – appointment of CAT Rapporteurs

Timetable:

-Final Briefing Package:	08.01.2021
-Start of the procedure at SAWP:	11-14.01.2021
-CAT report due by:	18.01.2021
-CAT recommendation:	22.01.2021

5.2. CAT reports

5.3. List of Issues

No items

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

No items

6.3. Priority Medicines (PRIME) – Eligibility requests

6.3.1. Month 0 - Start of the procedure

Timetable for assessment:

Procedure start:	26.11.2020
SAWP recommendation:	14.01.2021
CAT recommendation:	22.01.2021
CHMP adoption of report and final recommendation:	28.01.2021

6.3.2. Month 1 – Discussion of eligibility

6.3.3. Month 2 – Recommendation of eligibility

6.3.4. Ongoing support

No items

7. Organisational, regulatory and methodological matters

7.1. Mandate and organisation of the CAT

7.1.1. CAT membership

France: Nathalie Morgensztejn - membership mandate (alternate) ended on 12 November 2020

Action: for information

The information was noted

7.1.2. Joint CHMP-CAT memberships

Scope: Joint CHMP-CAT membership, new mandate 2020-2023 for: Romaldas Mačiulaitis, Sol Ruíz, Bruno Sepodes, Jan Mueller-Berghaus and John Borg

Action: appointment of alternate to Sol Ruiz and Jan Mueller-Berghaus

Sol Ruiz nominated Marcos Timon as her alternate; Jan Mueller-Berghaus nominated Egbert Flory as his alternate. CAT appointed both alternate members.

CAT was informed that the next Policy 044 on conflicts of interest will enter in operation on 1 January 2021. All CAT members, alternates and experts will receive a request for updating their declaration of interest (DoI). All DoIs will have to be updated before the start of the January CAT meeting.

7.1.3. Accelerated assessment – update of the AA tool

Scope: presentation of the new template and review of the accelerated assessment (AA) tool for ATMPs and non-ATMPs

Action: for discussion

Information was provided on the next template for requesting AA that will also be merged with the AA briefing note/assessment report and for evaluation of this request.

An analysis of the experience with AA for non-ATMP and ATMP MAAs was presented. CAT discussed possible reasons for the substantial number of reversions from AA to a normal timetable during assessment.

7.1.4. Revision of the ATMP classification procedure

Scope: presentation of new procedure

Action: for information

The revised ATMP classification procedure was presented.

CAT proposed to go for a 'silent' adoption for non-controversial classifications. For controversial classifications, an early interaction between the EMA coordinator and the CAT coordinator is proposed.

7.2. Coordination with EMA Scientific Committees

No items

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

7.3.1. EMA – Review of Working Parties

CAT: Martina Schüssler-Lenz

Scope: feedback from the SciCoBo meeting that took place on 30 November 2020 on the review of activities of the working parties of the EMA

Action: for information

EMA provided feedback on the ongoing exercise to review the working parties. The aim is to make better use of the resources in the national competent authorities and EMA.

7.3.2. Correspondence with Alliance for Regenerative Medicine (ARM) on the use of master files and certification schemes for ATMP manufacturing in Europe

CAT: Sol Ruíz

Scope: Response from EMA/CAT to ARM on the use of master files and certification schemes for ATMP manufacturing in Europe

Action: for discussion

Note: this topic was discussed previously in BWP in June 2020 and CAT in July 2020

The background of the letter from ARM was presented, and the response letter was discussed and agreed. The letter will be sent under the signature of the BWP and CAT chairs.

7.3.3. Guideline on quality, non-clinical and clinical aspects on medicinal products containing genetically modified cells

CAT: Martina Schüssler-Lenz

Scope: Amendment to section 6.5 (Clinical efficacy) following comments provided by Oncology and Biostatistics Working Party.

Action: for discussion

Note: this guideline was adopted by CAT in October 2020 and CHMP in November 2020. Publication has been put on hold to allow re-discussion of the clinical efficacy section

The proposed change to section 6.5 was presented. The rationale for the change was explained. CAT agreed with the change proposed.

CAT was made aware that additional amendments to improve the clarity of the text are proposed by the Oncology Working Party (OncWP). It was agreed that the chairs of the CAT and OncWP will review these changes and decide on their implementation: if changes are considered substantial, the revised guideline will be sent to CAT for adoption via a written procedure.

Post-meeting note: the proposed changes will be presented and discussed at the January plenary CAT meeting.

7.4. Cooperation within the EU regulatory network

7.4.1. Inspection of manufacturers of viral vectors used as starting materials for genetically modified cells

CAT drafting group members: Heli Suila, Ivana Haunerova, Marcos Timón, Violaine Closson Carella

Scope: draft Q&A on principles for GMP

Action: for discussion

Due to time constraints, the draft Q&A was not discussed. CAT members were asked to provide written comments by 18 December 2020.

This topic will be discussed at the January 2021 CAT meeting.

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

CAT: Martina Schüssler-Lenz

Scope: inception impact assessment on the revision of the BTC legislation

Action: for discussion

Note: the European Commission has opened the inception impact assessment for feedback by 14 December 2020.
A presentation was given by the European Commission representative from DG SANTE, Unit B4, responsible to Substance of Human Origin on the reasons for revision of the BTC legislation.

During the subsequent discussion, CAT members raised following comments:

1. Unclarity of the scope of the exercise. CAT considered that (cell-based) ATMPs should be excluded from this revision, as they are considered, as medicinal products. As for all medicines, the safety and efficacy of ATMPs have to be demonstrated in a clinical trial, and

this is considered essential to protect patients from the use of non-efficacious, unsafe ATMP (reference is made to the Stamina case, and the use of Wharton jelly derived MSC for a variety of indications, some of them even requiring intrathecal injection). In that respect, CAT issued in April 2020 a statement advising patients and the general public against using unregulated cell-based therapies which may not be safe or effective[1]. CAT is therefore of the strong opinion that the regulatory standard for ATMPs should not be changed or lowered in any way. A deregulation of ATMPs (via extension of the scope of the future BTC legislation) would be contrary to Public Health.

2. Classification of borderline products. CAT considered that a well functioning system, the ATMP classification procedure, is already operational in the EU (almost 500 classifications issued so far). ATMP classification are hardly ever disputed by developers or authorities. If needed, the scope of the current ATMP classification procedure can be expanded so that it can be used by blood and tissue establishments instead of setting up a separate classification system under the BTC legislation.

Further to these comments, the Commission representative recognised these concerns and clarified that the revision does not aim to alter the ATMP framework. Rather common work is needed to clarify the borderline and to improve interplay between the 2 sectors. This will help achieve the common aim to ensure access to safe and effective therapies for patients.

As regards the next steps, the Commission informed that the CAT's input will be particularly important during the public consultation and the targeted stakeholder consultation which will be opened for 12 weeks at the end of 2020/beginning of 2021 in order to inform the legislative impact assessment. That process will focus on the exact details of how the EU should organise the new framework. Alongside these consultations, a third party contractor has been selected by the Commission to prepare an impact assessment study to better understand the impact of the different policy options described in the inception impact assessment, their costs and to compare them. This study will also aim to complement the findings of the 2019 evaluation to take into account the lessons learnt from COVID-19. The study will include an expert workshop in Q1 2021 and several in-depth interviews on dedicated topics, including with CAT members. Such interviews will also focus on borderline issues and assess what they mean for the pharmaceutical, medical device and BTC frameworks. The Commission will organise several bilateral meetings with relevant stakeholders, all publicly minuted, to better investigate relevant issues, including with EMA.

DG SANTE will make sure to keep CAT informed and will invite CAT to the different meetings and interviews mentioned.

CAT expressed his willingness to work with the Commission in order to address the concerns and to contribute to the revision of the BTC legislation

It was agreed to provide a CAT feedback on the inception impact assessment highlighting the concerns raised during the discussion.

CAT members were asked also to comment on the inception impact assessment from their NCAs (deadline: 14 December 2020): the CAT position can form the basis of their feedback.

7.4.3. Heads of Medicines Agencies (HMA)-EMA joint big data – Big data training signpost

Action: for discussion

Note: the Big Data training signpost is a collection of external training courses on Big Data skills that we believe can benefit the network until the Big Data curriculum is ready which will contain tailor-made and more targeted trainings instead.

EMA provided feedback on the big data training signpost. CAT discussed how this exercise would fit with the ATMP training curriculum.

It was proposed to have a discussion in the January CAT meeting on the ATMP training curriculum, with the aim to identify where training is needed and how the big data training will fit in.

[1] https://www.ema.europa.eu/en/documents/public-statement/ema-warns-against-using-unproven-cell-based-therapies_en.pdf

7.4.4. Multi-stakeholder webinar to support implementation of the Medical Devices Regulation on drug-device combinations

CAT: Ilona Reischl

Scope: feedback from the workshop and implications for ATMPs

Action: for discussion

Note: information on the multistakeholder webinar can be found here: https://www.ema.europa.eu/en/events/multi-stakeholder-webinar-support-implementation-medical-devices-regulation-drug-device-combinations

A short feedback from the workshop was provided.

7.4.5. Regulatory status of Ribonucleic acid (RNA) products

CAT: Marcos Timón, Violaine Closson-Carella, Egbert Flory, Hans Ovelgönne

Scope: reflection on the consequences for ATMPs of the Commission's feedback on the regulatory status of RNA products in the context of vaccines against COVID-19

Action: for discussion

Further to a discussion in July 2020 (see CAT minutes of the July CAT meeting, point 7.4.2), a brainstorming meeting took place (between CAT secretariat and CAT members) to reflect upon the consequence for the ATMP field of the Commission's feedback on a question from EMA on the status of RNA vaccines that are prepared fully synthetically.

Feedback from the brainstorming meeting was provided. For the moment, messenger RNAs (mRNA) are produced biosynthetically (transcribed in vitro for a DNA template) and fulfil the definition of a GTMP: such long chain mRNAs cannot yet be produced via chemical synthesis. However, when this becomes possible, the regulatory status of such synthetic RNAs need to be considered, as it should be avoided to have similar products being covered by different legal frameworks.

In the field of genome editing, some settings (i.e. in vivo genome editing based on the administration of the nuclease (enzyme) and a synthetic guide RNA) are currently not covered by the definition of a GTMP: this should be kept in mind if the GTMP definition would be opened for revision (see 7.5.2).

7.5. Cooperation with international regulators

7.5.1. ATMP cluster teleconference with FDA-USA, Health Canada and PMDA-Japan

CAT: Martina Schüssler-Lenz

Scope: feedback on the teleconference that took place on 12 November 2020

Action: for information

A short feedback was provided of the last ATMP cluster teleconference.

7.5.2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) – ICH-S12 guideline

CAT: Rune Kjeken, Claire Beuneu

Scope: feedback on the development of the ICH-S12 guideline: Nonclinical Biodistribution Studies for Gene Therapy Products

Action: for discussion

The EU Rapporteurs (Claire Beuneu and Rune Kjeken) provided detailed information on the progress of the development of this ICH guideline. Input from the core group identified at the

February 2020 CAT meeting[2] on the principles/concepts is sought: their feedback to the EU Rapporteurs is awaited in January 2021.

The EU Rapporteurs also informed CAT that the ICH drafting groups have agreed to include a definition of GTMP in the glossary of the guideline: this definition is not in line with the GTMP definition that is included in the EU legislation. Apparently, other ICH regions/countries do not have a definition of GTMP in their legislation (but rather in guideline), and therefore have less problems with adapting their definition to the one in the ICH guideline: for EU, a revision of the legal GTMP definition would be needed.

CAT agreed that it would be good to start reflecting on a revision of the GTMP definition, with the aim of adapting it to the current state of science: for example, it would be good that genome editing approaches are reflected in the future GTMP definition (see also 7.4.5).

7.5.3. International Pharmaceutical Regulators Programme (IPRP) – Gene therapy working group

CAT: Pille Säälik

Scope: feedback from the teleconference that took place on 12 November 2020

Action: for discussion

A short feedback was provided of the last IRPR – gene therapy working group teleconference.

7.6. CAT work plan

7.6.1. CAT work plan 2021

Scope: draft CAT work plan 2021

Action: for discussion

The draft work plan for 2021 was presented. CAT agreed with the proposed work plan (WP) topics and additional committee participants for the topics were identified.

CAT was informed of the next steps: next week, an internal discussion will take place to align to the WPs of other Committee and to reflect on the feasibility in the light of the current BCP/Corona Pandemic situation (reduction of the number of work plan topics could be proposed). The draft WPs will then be presented at the SciCoBo meeting that will take place on 14 December 2020. Adoption of the CAT WP 2021 will take place at the January 2021 plenary meeting.

7.7. Planning and reporting

7.7.1. Planning estimates of forthcoming ATMP MAAs

Scope: Q4/2020 update of the business pipeline report for the human scientific committees

Action: for information

The information was noted.

[2] Following members and expert will contribute to this activity: Anne Pastoft, Egbert Flory, Brigitte Anliker, Tineke van den Hoorn. Isabel Vieira agreed to be part of this core group.

7.8. Others

7.8.1. Process for documenting of CAT experiences / CAT learning

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

Scope: Process for collecting and maintaining CAT learnings and presentation of CAT learnings: ‘

Action: for discussion

This topic was postponed due to time constraints. CAT members were asked to review of draft CAT learnings in the tracking table, in advance of discussion in the January 2021 CAT meeting.

8. Any other business

No items

Date of next CAT meeting:

20-22/01/2021

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: Scientific Working Party

SME: Small and medium size enterprises

SmPC: Summary of Products Characteristics

TT: Timetable

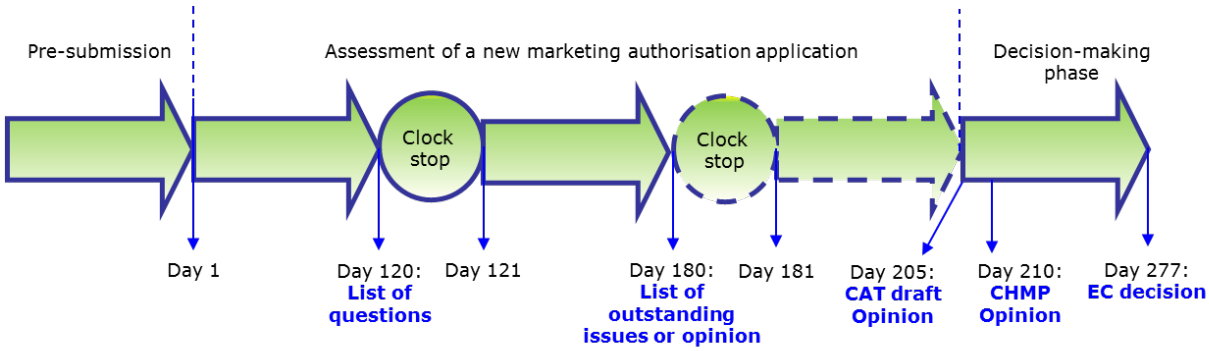
Evaluation of ATMPs (section 2)

This section lists applications for marketing authorisations of new Advanced Therapy Medicinal Products (ATMPs) that are to be discussed by the Committee. It also lists any ATMP related inspection requests (section 2.9) and Post-authorisation activities (section 2.10).

New applications (sections 2.1. to 2.12.)

Section 2.1 is for ATMPs nearing the end of the evaluation and for which the CAT is expected to adopt a draft **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CAT opinion is transmitted to the CHMP for final adoption. The CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU. More information on the evaluation of ATMPs can be found here.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CAT. The clock stop happens after day 120 and may also happen after day 180, when the CAT has adopted respectively a **Day 120 list of questions** (section 2.3) or a List of outstanding issues to be addressed by the company, which is listed in the agenda under sections 2.7 (**Ongoing evaluation procedures**). Section 2.7 also includes the CAT discussions at any other timepoint of the evaluation procedure of new applications.

Oral explanation (section 2.2.)

Prior to adoption of the CAT opinion, marketing authorisation applicants are normally invited to the CAT plenary meeting to address questions raised by the Committee.

Oral explanations normally relate to ongoing applications, but they can also relate to any other issue for which the CAT would like to discuss with company representatives in person.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 (section 2.6.)

This section lists applications for new marketing authorisation for ATMPs for which the applicant has requested a re-examination of the opinion previously issued by the CHMP. Similar to the initial evaluation of a marketing authorisation of an ATMP, CAT will adopt a draft re-examination opinion, which is transmitted to the CHMP for final adoption.

Withdrawal of applications (section 2.7.)

This section includes information on marketing authorisation applications that are withdrawn by the applicant. Applicants may decide to withdraw applications at any stage during the assessment and a CAT opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

New applications (section 2.9.)

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

GMP and GCP Inspections Issues (section 2.10.)

This section lists inspections that are undertaken for ATMPs. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Post-authorisation activities (section 2.12.)

This section lists type II variations, extension application according to Annex I of Reg. 1234/2008, re-examination procedures for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP and other issues concerning authorised medicines that are not covered elsewhere in the agenda such as annual reassessments, 5-year renewals, supply shortages, qualify defects. Issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines, will also be included here.

Certification of ATMPs (section 3)

This section includes the scientific evaluation by the CAT of quality and non-clinical data that small and medium-sized enterprises have generated at any stage of the ATMP development process. More information on the ATMP certification procedure can be found here.

Scientific Recommendation on Classification of ATMPs (Section 4)

This section includes the scientific recommendation by the CAT on whether medicines based on genes, cells or tissues meet the scientific criteria that define ATMPs. More information on the ATMP classification procedure, including the outcomes of finalised classifications, can be found here.

Scientific Advice (section 5)

This section includes all scientific advice given to companies during the development of an ATMP. Information related to the number of ATMP related scientific advices discussed by CAT can be found in the CAT Monthly reports. Further information on SAWP can be found here.

Pre-Authorisation (section 6)

Paediatric Investigation Plan (PIP)

This section includes the discussion of an ATMP before a formal application for marketing authorisation is submitted. These cases refer for example to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation: in case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

CAT contributes to the evaluation of a Paediatric Investigation Plan (PIPs) for ATMPs by the Paediatric Committee. These PIPs are included in this section of the Agenda.

ITF Briefing meeting in the field of ATMPs

This section refers to briefing meetings of the Innovation Task Force and International co-operations activities of the CAT

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes of meetings with applicants developing ATMPs and of other ITF meetings of interest to the CAT are included in this section of the agenda. Further information on the ITF can be found here.

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 02-04 December 2020 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	
Mirna Golemovic	Member	Croatia	No interests declared	
Petra Sokol	Alternate	Croatia	No interests declared	
Isavella Kyriakidou	Alternate	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	
Olli Tenhunen	Alternate	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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Angeliki Rompoti	Alternate	Greece	No interests declared	
Katalin Lengyel	Member	Hungary	No interests declared	
Maura O'Donovan	Member	Ireland	No interests declared	
Niamh Curran	Alternate	Ireland	No restrictions applicable to this meeting	
Paolo Gasparini	Member	Italy	No interests declared	
Giulio Pompilio	Alternate	Italy	No restrictions applicable to this meeting	
Una Riekstina	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member (CHMP member)	Lithuania	No interests declared	
Raimondas Benetis	Alternate (to CHMP representative)	Lithuania	No interests declared	
Guy Berchem	Member	Luxembourg	No restrictions applicable to this meeting	
Anthony Samuel	Alternate (to CHMP representative)	Malta	No interests declared	
Carla Herberts	Member	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Alternate	Netherlands	No interests declared	
Rune Kjeken	Member	Norway	No restrictions applicable to this meeting	
Maja Sommerfelt Grønvold	Alternate	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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Felicia Ciulu-Costinescu	Member	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	
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	2.13.1. and 2.13.2.
Alessandra Renieri	Alternate	Healthcare Professionals' Representative	No interests declared	
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	
Giuseppa Pistritto	Expert - remotely	AIFA-IT	No interests declared	
Bjørg Bolstal	Expert - remotely	NOMA-NO	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Helga Haugom Olsen	Expert - remotely	NOMA-NO	No interests declared	
Hilde Røshol	Expert - remotely	NOMA-NO	No interests declared	
Johanna Lähteenvuo	Expert - remotely	FIMEA-FI	No interests declared	
Karri Penttilä	Expert - remotely	FIMEA-FI	No interests declared	
Daiana Vasilcanu	Expert - remotely	MPA-SE	No interests declared	
Annika Folin	Expert - remotely	MPA-SE	No interests declared	
Blanca Garcia-Ochoa	Expert - remotely	AEMPS-ES	No interests declared	
Rosalía Ruano	Expert - remotely	AEMPS-ES	No interests declared	
Ralf Tönjes	Expert - remotely	PEI-DE	No restrictions applicable to this meeting	
Jürgen Scherer	Expert - remotely	PEI-DE	No interests declared	
A representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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