Advanced therapy medicinal products (ATMPs): regulatory framework, development & marketing authorization in the EU

Ca' Foscari University of Venice - Department of Molecular Sciences and Nanosystems

July 8th, 2026

Barbara Bonamassa, PhD

Innovation and Pharmaceutical Strategy Department - Italian Medicines Agency (AIFA)

Italian Alternate Member at the Committee for Advanced Therapies (CAT)

Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	X	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	X	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	X	☐	☐	☐ optional
2. Consultancy for a company	☐	☐	☐	X
3. Strategic advisory role for a company	X	☐	☐	☐ optional
4. Financial interests	X	☐	☐	☐ optional
5. Ownership of a patent	X	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	X	☐	☐	☐ optional
7. Investigator	X	☐	☐	☐ optional
8. Grant or other funding	X	☐	☐	☐ optional
9. Family members interests	X	☐	☐	☐ optional
10. Serious reasons of convenience	X	☐	☐	☐ optional

*Barbara Bonamassa, in accordance with the Regulation for the prevention and handling of conflicts of interest of the Italian Medicines Agency, approved by AIFA Board of Directors (Resolution no. 9 - 12 February 2025).

N.B. I am not receiving any compensation

The views expressed in this presentation are those of the speaker, and may not be understood or quoted as being the official opinion of AIFA, EMA or any of its Committees.

- Advanced therapy medicinal products (ATMPs) definitions,
- Overall regulatory framework for ATMPs,
- ATMPs evaluation & access pathways:

- the hospital exemption (HE) framework,

- the clinical trial framework,

- the Marketing Authorization (MA) framework & the Committee for Advanced Therapies (CAT),

- Additional regulatory and scientific support tools specific to the development/commercialization of ATMPs,
- Examples of approved ATMPs.

"The **EU legal framework** for human medicines sets standards to ensure a high level of **public health protection** and the **quality, safety and efficacy** of authorized medicines.

In addition, it promotes the **functioning of the internal market**, with measures to **encourage innovation**.

It is based on the principle that a **medicinal product requires a marketing authorization by the competent authorities** before being placed on the market."

↓

DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 November 2001

on the Community code relating to medicinal products for human use

Medicinal product definition:

a) Any substance or combination of substances presented as having properties for **treating or preventing disease** in human beings;

or

b) Any substance or combination of substances which may be used in or administered to human beings either with a view to **restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis**.

↓

The regulatory framework for human medicinal products applies, ensuring **quality, safety and efficacy** (appropriate regulatory evaluations undertaken).

Directive 2001/83/EC, Annex I - Part IV → early specific **definitions** for 'gene-therapy medicinal product' (GTMPs) and 'somatic cell-therapy medicinal product' (sCTMPs).

Directive 2009/120/EC (amending Directive 2001/83/EC) → **updated** specific definitions.

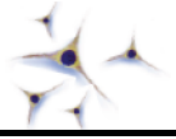
1) *"**Gene therapy medicinal product** means a **biological medicinal product** which has the following characteristics:*

*(a) it contains an active substance which contains or consists of a **recombinant nucleic acid** used in or administered to human beings with a view to **regulating, repairing, replacing, adding or deleting a genetic sequence**; **and***

*(b) its therapeutic, prophylactic or diagnostic effect **relates directly to the recombinant nucleic** acid sequence it contains, or **to the product of genetic expression of this sequence**.*

Gene therapy medicinal products shall not include vaccines against infectious diseases".

CAT framework under revision (Revision of the EU general pharmaceuticals legislation - EU pharmaceuticals strategy (https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en)).

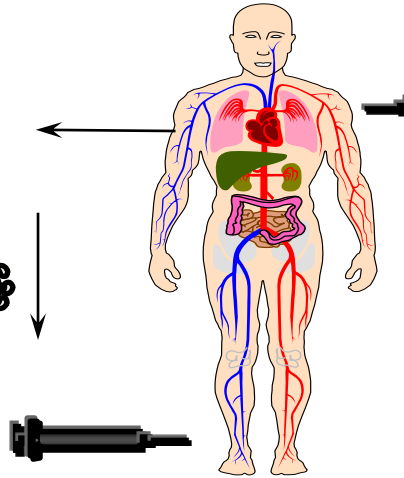
Recombinant nucleic acid sequences	•Oligonucleotides (of biological origin) •Plasmid DNA •Naked or formulated (lipids, polymers, peptides
Genetically modified viruses	•Replication deficient/competent •Conditionally competent
Genetically modified microorganisms	•Mycobacterium bovis, Shigella, Clostridium
Genetically modified cells 	•Autologous, allogenic, xenogenic •Primary or cell lines

ex vivo

Collection + preparation of target cells

Genetic modification

Infusion of genetically modified cells (autogous, allogeneic.)



in vivo

Direct Application:

Viral vector

Non-viral vector

Naked DNA

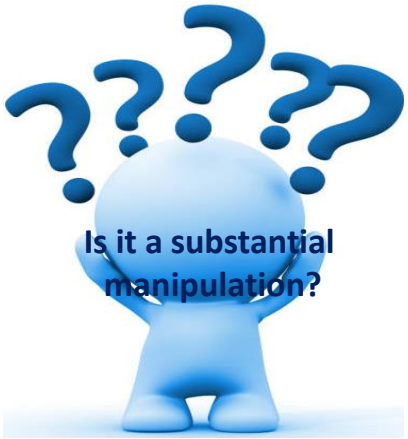
2) Somatic cell therapy medicinal *product means a* ***biological medicinal product*** *which has the following characteristics:*

(a)contains or consists of cells or tissues *that have been subject to* ***substantial manipulation*** *so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered,* ***or*** *of cells or tissues that are* ***not intended to be used for the same essential function(s)*** *in the recipient and the donor;* ***and***

(b) is presented as having properties for, or is used in or administered to human beings with a view to ***treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues****".*

• Substantial manipulations (examples): cell expansion (culture), genetic modification of cells, differentiation/activation with growth factors, etc.

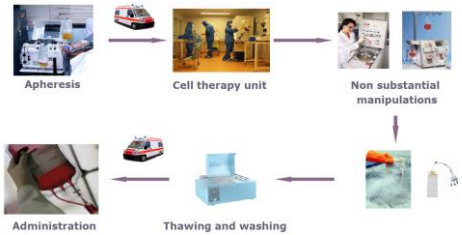
• **Not** a substantial manipulation: cutting, grinding, shaping, centrifugation, soaking in antibiotic or antimicrobial solutions, sterilization, irradiation, cell separation, concentration or purification, filtering, lyophilization, freezing, cryopreservation, vitrification.



• Enzymatic digestion:
Yes, if cell-cell contacts are dissociated, *e.g.*, keratinocytes from skin.
No, if functionally intact tissue units are isolated, *e.g.*, pancreatic islets.

• Enrichment:
No, if the number of certain cells, e.g., MSCs in fat grafts, is enriched by selection and the processing does not change the characteristics of the cells.

The same essential function for a cell population means that the cells when removed from their original environment in the human body are used to maintain the original function(s) in the same anatomical or histological environment.



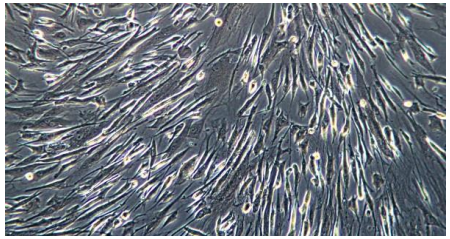
Bone marrow cells or peripheral blood cells used for haematopoietic or immune reconstitution

↓

same essential function (homologous use), non substantial manipulation

↓

Not ATMP (transplant)



Autologous human MSCs present in bone marrow cells suspension used for the treatment of type 2 diabetes mellitus.

↓

Different essential function, non substantial manipulation

↓

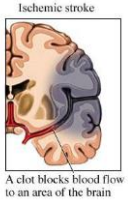
ATMP

Regulation (EC) No 1394/2007 → **Tissue engineered products** (TEPs)

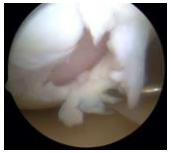
"A product that:
*-contains or consists of **engineered** cells or tissues, **and***
*-is presented as having properties for, or is used in or administered to human beings with a view to **regenerating, repairing or replacing a human tissue**.*
***A tissue engineered product may contain cells or tissues** of human or animal origin, or both. The cells or tissues **may be viable or non-viable**. It may also contain additional substances, such as cellular products, bio-molecules, biomaterials, chemical substances, scaffolds or matrices. **Products containing or consisting exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and which do not act principally by pharmacological, immunological or metabolic action, are excluded from this definition**.*

*Cells or tissues shall be considered '**engineered**' if they fulfill **at least one** of the following conditions:*
*-the cells or tissues have been subject to **substantial manipulation**, so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved.*
*- the cells or tissues are **not intended** to be used **for the same essential function** or functions in the recipient as in the donor."*

In vitro cultured autologous mesenchymal stem cells isolated from bone marrow



Intended for the treatment of ischemic stroke.



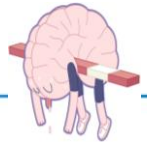
Intended for regeneration of cartilage, ligaments and bone and muscle defects

TEPs

sCTMPs vs TEPs

They both contain cells or tissue. They differ in the intended use:

- sCTMPs: treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues,
- TEPs: regenerating, repairing or replacing a human tissue.



More definitions...

- Regulation (EC) No 1394/2007 → Combined ATMPs

- Reflection paper on classification of advanced therapy medicinal products

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

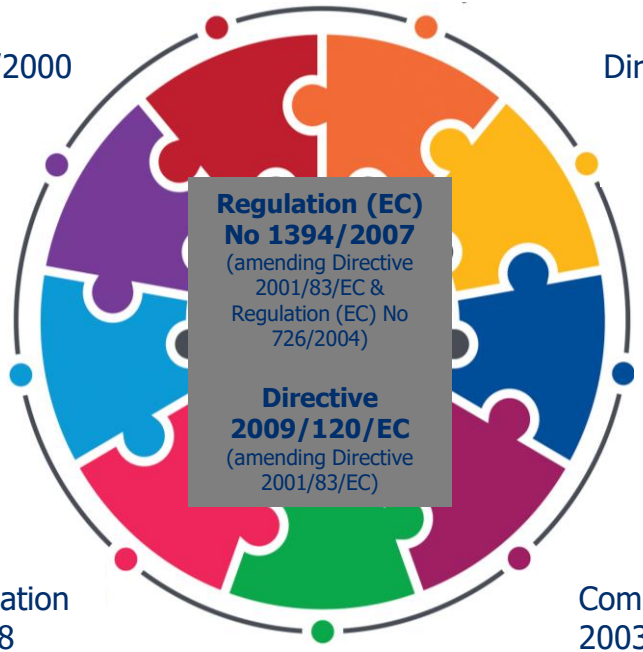
21 May 2015
EMA/CAT/600280/2010 rev.1
Committee for Advanced Therapies (CAT)

Reflection paper on classification of advanced therapy medicinal products

Directive 95/46/EC

Regulation (EC) No 141/2000
Commission Regulation
(EC) No 847/2000

Directive 2001/18/EC



Directive 2004/23/EC
Directive 2002/98/EC
(and implementing directives)

Regulation EU
No 536/2014

PhV legislation
(Regulation (EU) No 1235/2010 & 1027/2012
Directive 2010/84/EU & 2012/26/EU
Commission Implementing Regulation No 520/2012)

Commission Directive
2005/28/EC

Commission Regulation
(EC) No 1234/2008

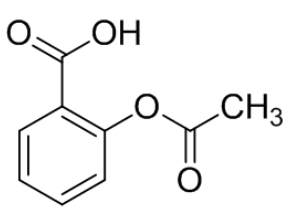
Commission Directive
2003/94/EC

Regulation (EC) No 1901/2006
Regulation (EC) No 1902/2006

...As adapted to ATMPs

Legal framework: Advanced therapies: https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapies/legal-framework-advanced-therapies

The Beauty and the Beast
Genes
Cells
You can be anything you want to be when you grow up.
STEM CELL PARENTAL ADVICE
BIZARROCOMICS.COM Facebook.com/BizarroComics
Cell-fie


O
OH
O
CH3
O

Regulation (EC) No 1394/2007: a *lex specialis* (2)

10.12.2007 EN Official Journal of the European Union L 324/121

REGULATION (EC) No 1394/2007 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 13 November 2007

on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004

(Text with EEA relevance)

ATMPs complexity ⟶ additional provisions to those laid down in Directive 2001/83/EC for ATPMs intended for marketing manufactured industrially or by a method involving an industrial process, to ensure:

- free movement of ATMPs within the Community, and the effective operation of the internal market in the biotechnology sector,
- very specific expertise for ATMPs evaluation,
- flexibility in ATMPs evaluation.

• ATMPs

– Definitions → ATMPs are medicinal products.

• Principles of existing legislation on medicines (Directive 2001/83/EC) apply to ATMPs:

– demonstration of quality, safety & efficacy,
– marketing authorization,
– ATMPs are authorized in the EU via the centralized procedure,
– GMP & GCP apply, adapted to ATMPs,
– post-authorisation follow-up of both efficacy & safety.

• Sets up a dedicated Committee, the Committee for Advanced Therapies (CAT).

- (High level) Scientific and technical requirements for ATMPs,
- risk-based approach (risks & innovation).

Due to the specific nature of advanced therapy medicinal products, a risk-based approach may be applied to determine the extent of quality, non-clinical and clinical data to be included in the marketing authorisation application, in accordance with the scientific guidelines relating to the quality, safety and efficacy of medicinal products referred to in point 4 of the "Introduction and general principles".

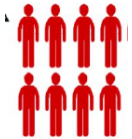
The risk analysis may cover the entire development. Risk factors that may be considered include: the origin of the cells (autologous, allogeneic, xenogeneic), the ability to proliferate and/or differentiate and to initiate an immune response, the level of cell manipulation, the combination of cells with bioactive molecules or structural materials, the nature of the gene therapy medicinal products, the extent of replication competence of viruses or micro-organisms used *in vivo*, the level of integration of nucleic acids sequences or genes into the genome, the long time functionality, the risk of oncogenicity and the mode of administration or use.

Relevant available non-clinical and clinical data or experience with other, related advanced therapy medicinal products may also be considered in the risk analysis.

- Allogeneic cells: risk of disease transmission, unwanted immunogenicity, Graft Versus Host Disease, etc
- Impact of the manufacturing process on cells: e.g., quality characteristics & manufacturing success rate, tumourigenicity profile,
- Storage, distribution and reconstitution of the ATMPs at administration site,
- Administration procedure: e.g., surgery,
- Patient related-aspects: e.g., conditioning regimen, immunosuppression, concomitant treatments, underlying disease,
- Persistence of the ATMPs in the patient: long-term follow-up to monitor both safety & efficacy (up to 15 years),
- GTMPs: e.g., risk of insertional mutagenesis,
- Shedding, ERA, risks for HC professionals, care givers & unintended recipients.

Guidelines relevant for advanced therapy medicinal products:
https://www.ema.europa.eu/en/human-regulatory/research-development/advanced-therapies/guidelines-relevant-advanced-therapy-medicinal-products

Hospital exemption (so-called «special use»)	Clinical trial setting	Marketing authorization setting
Single patient	Cohort of patients	Many patients



Regulatory & technical-scientific evaluation & authorizazion by the relevant Competent Autority (AIFA/EMA) is required.

Article 28(2) of the Regulation EU No 1394/200 "ATMP Regulation"
Article 3
(7) of Directive 2001/83

Empowers EU Member States to authorise the manufacturing and administration to patients of ATMPs under **certain conditions**, subject to legislation
implemented at the national level

- must be prepared on a non-routine basis
- according to specific quality standards
- for an individual patient
- used within a hospital setting within the same Member State in which they are manufactured under the exclusive professional responsibility of a medical practitioner

The HE framework is a **derogation**: it allows the manufacturing and use of ATMPs in Member States, without requiring & obtaining a marketing authorization as instead foreseen by the EU pharmaceutical legislation, under specific conditions. However, it necessitates authorization by NCAs and compliance with certain national requirements related to traceability, quality and pharmacovigilance.

Italian regulatory framework*: D.M. 16 gennaio 2015 Disposizioni in materia di medicinali per terapie avanzate preparati su base non ripetitiva:*

- Lack of suitable therapeutic alternative,
- Clinical case of urgency and emergency,
- AIFA authorization for manufacture,
- AIFA authorization for clinical use,
- Quality & clinical monitoring provisions.

9 authorisation holders
(organisation type – type of authorisation)

IRCCS Ospedale San Raffaele
(Research Hospital – authorisation for use)

Holostem Therapie Avanzante S.r.l
(Company – authorisation for manufacturing)

ASST Monza – Ospedale San Gerardo – Laboratorio di Terapia Cellulare e Genica "Stefano Verri"
(Research centre – authorisation for manufacturing)

Azienda ULSS8 Berica – Laboratorio di Terapie cellulari Avanzate (LTCA)
(Research centre – authorisation for use and manufacturing)

Officina Farmaceutica Ospedale Pediatrico Bambino Gesù
(Hospital/ research centre - authorisation for use and manufacturing)

Fondazione I.R.C.C.S. Istituto Neurologico "Carlo Besta"
(Non-profit/ research centre - authorisation for use and manufacturing)

IRCCS Fondazione Policlinico San Matteo
(Research centre - authorisation for use and manufacturing)

MolMed S.p.A. (now AGC Biologics S.p.A.)
(Biotech company – authorisation for manufacturing)

Officina Rigenerand SRL
(Biotech company – authorisation for manufacturing)

(https://www.aifa.gov.it/en/uso-non-ripetitivo-di-terapie-avanzate;
(https://op.europa.eu/en/publication-detail/-/publication/b89eb680-7730-11f0-9af8-01aa75ed71a1/language-en?WT.mc_id=Selectedpublications&WT.ria_c=69089&WT.ria_f=7230&WT.ria_ev=search&WT.URL=https%3A%2F%2Fhadea.ec.europa.eu%2F; https://op.europa.eu/en/publication-detail/-/publication/b89eb680-7730-11f0-9af8-01aa75ed71a1/language-en))

- Regulatory framework for ATMPs: parallel systems with no regulatory overlap,

Centrally authorised ATMPs

Clinical trials with investigational ATMPs

Hospital exemption

- Advantages & limitations of the HE scheme,

Provide access to patients with innovative, potentially life-saving treatments

- Success stories confirm the therapeutic effect and quality of HE ATMPs: the case CAR-T ARI 0001 of the Hospital Clinic of Barcelona
- The number of patients that have been treated by hospital ATMP preparations

The recognition and interpretation of the provision in MS differs substantially:

- Definition of "non-routine basis"
- Manufacturing
- Clinical data requirements
- Lack of reporting & transparency of use

- Criticalities: divergence in the national rules for HE, clinical evidence for HE authorization, limitations in use in terms of number of patients, continuation of supply of ATMPs developed in hospitals when commercial ATMPs are authorised (central MA), etc.
- HE framework under revision (Revision of the EU general pharmaceuticals legislation - EU pharmaceuticals strategy).

Hospital exemption (HE) – Dr. Koufokotsiou L. (https://express.converia.de/frontend/index.php?page_id=25930) - Scientific and Regulatory Aspects of Innovative Gene Therapy Medicinal Products - Paul-Ehrlich-Institut (PEI) Workshop, September 27th, 2022; Study on the hospital exemption – European Commision (https://op.europa.eu/en/publication-detail/-/publication/00dd95c5-766d-11f0-9af8-01aa75ed71a1/language-en)

ATMP DEVELOPMENT

MARKETING AUTHORISATION

POST-APPROVAL LIFE CYCLE MANAGEMENT, PHARMACOVIGILANCE

Clinical Trials

Clinical trial authorisation

CAT

PRAC

CHMP

Benefit-risk assessment / opinion

(Conditional) Approval

Post-authorisation data generation,
Real World Data,
Clinical trials, indication extension

HTAs, Reimbursement

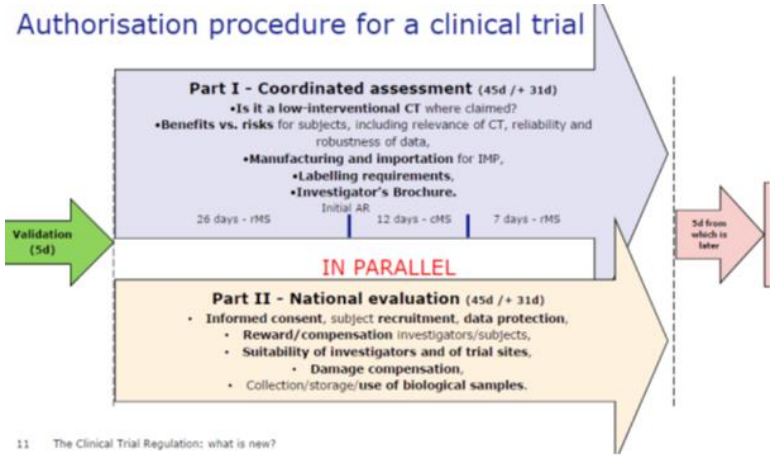
Patient access

RWD

Scientific assessments and authorisations by experts from NCAs throughout life cycle

The life cycle management of Advanced Therapy Medicinal Products (ATMPs) – a regulatory perspective– Dr. Schuessler-Lenz M. (https://express.converia.de/frontend/index.php?page_id=25930)
Scientific and Regulatory Aspects of Innovative Gene Therapy Medicinal Products - Paul-Ehrlich-Institut (PEI) Workshop, September 27th, 2022

- Clinical Trial Regulation (CTR) 536/2014: From 31 January 2023, clinical trial sponsors will need to use EU database (CTIS) for all initial CTA in the EU/EEA.



- Harmonized:

- facilitate conduct of large clinical trials in multipe EU member states,
- single application and procedure,
- assessment by national competent authorities - co-ordinated multinational assessment.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 January 2025
EMA/CAT/22473/2025
Committee for Advanced Therapies (CAT)

Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials

(https://www.ema.europa.eu/en/guideline-quality-non-clinical-clinical-requirements-investigational-advanced-therapy-medicinal-products-clinical-trials-scientific-guideline)

General points on the Guideline

- Multidisciplinary guideline (Q, NC &C) for all iATMPs (SCMP, TEP, GTMP) - intended as stand-alone document,
- cross-references where relevant, especially the Guideline on GMP for ATMPs and GLs for MAA for late-stage development,
- guidance is by principles rather than "cooking recipes" – due to ATMP heterogeneity,
- joint text for all iATMPs, where applicable, and split where needed,
- Common Technical Document (CTD) structure/headings,
- differentiation into exploratory/confirmatory trials (rather than phases) development stage appropriate data & requirements,
- a risk-based approach can be applied throughout ATMP development the extent of the Q, NC & C data can be adapted to potential risks identified for the investigated product. The risk analysis should be updated as new data become available,
- priority needs to be given to the safety of trial participants and the robustness of data as per Regulation (EC) No 536/2014.

- Harmonized:

Ethics Committee specific for ATMPs established in Italy (HE and compassionate use assessment excluded):

Decreto del Ministro della salute 3 marzo e 4 aprile 2025 di nomina dei componenti del Comitato etico per le sperimentazioni cliniche relative alle terapie avanzate presso l'AIFA

- **Not** harmonized:

- CTs with genetically modified organism (GMO) - approval by national GMO authorities required (Directive 2001/18/EC and/or Directive 2009/41/EC),
- no harmonization of GMO authorisation procedure,
- GMO evaluation not adjusted in the CTR (Article 91 of CTR),
- not possible to submit any GMO documentation via CTIS,
- a step toward harmonization….good practice document on the GMO-related aspects assessment & common application form to be used for authorisation under the GMO framework (https://health.ec.europa.eu/medicinal-products/advanced-therapies_en)

CAT framework under revision (Revision of the EU general pharmaceuticals legislation - EU pharmaceuticals strategy (https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en)).

The Committee for Advanced Therapies (CAT)

(a) five members or co-opted members of the CHMP coming from five Member States, with alternates;

(b) one member and one alternate appointed by each EU Member State whose national competent authority is not represented among the members and alternates appointed by CHMP;

(c) one member and one alternate appointed by their respective Member States from the EEA/EFTA (Iceland, Liechtenstein, Norway);

(d) two members and two alternates to represent clinicians;

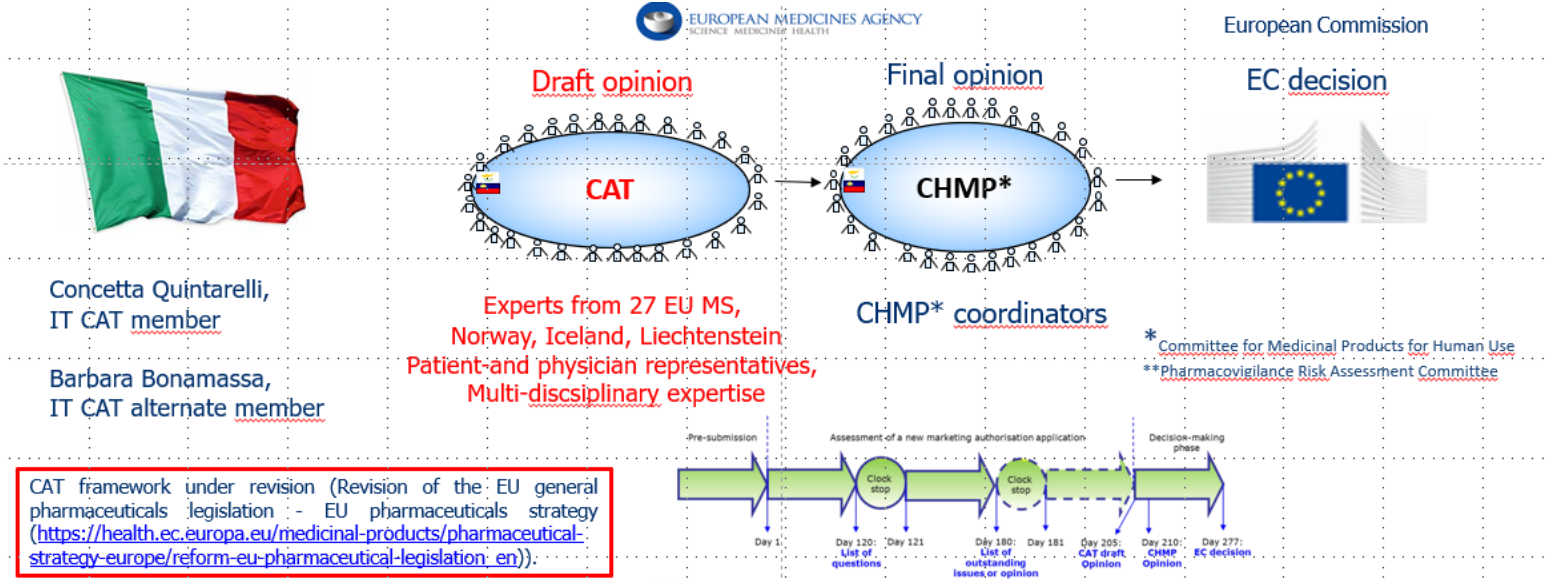
(e) two members and two alternates appointed to represent patients' associations.

CAT framework under revision (Revision of the EU general pharmaceuticals legislation - EU pharmaceuticals strategy (https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en)).

(https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat)

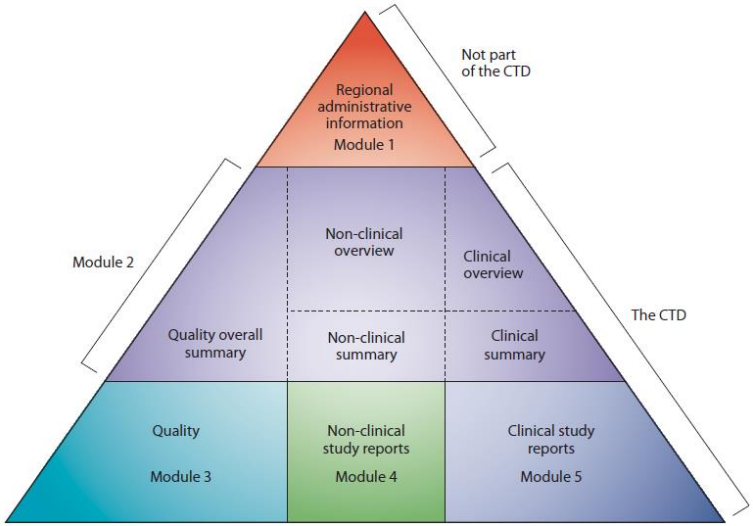
- Centralised MA:

- one license valid in entire EU/EEA (Regulation (EC) 1394/2007/EC & 726/2004),
- 210-day procedure (or 150 days, as applicable),
- CAT assessment & draft opinion -- Committee for Medicinal Products for Human - Use (CHMP) final opinion -- EC decision -- granting of the MA.



(https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat)

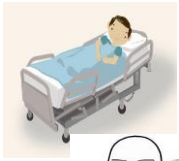
- Primary CAT responsibility for ATMPs MAA: assessment for the full dossier, i.e., quality (M3), non-clinical (M4), clinical (M5) & post-authorization measures:



Module 3 (quality)
manufacturing process validation [DS/DP (in case of GMCs, RVV/LVV starting material)],

Module 4 (non clinical)
pharmacology,
pharmacokinetics (biodistribution),
toxicology.

Module 5 (clinical)
clinical efficacy & safety



Is the benefit/risk ratio positive?

Guidelines relevant for advanced therapy medicinal products:
https://www.ema.europa.eu/en/human-regulatory/research-development/advanced-therapies/guidelines-relevant-advanced-therapy-medicinal-products

PRIority Medicines (PRIME) scheme

PRIME: in brief

Medicines eligible for PRIME must address an unmet medical need.

Preliminary data must be available showing the potential to address this need and bring a major therapeutic advantage to patients.

EMA will provide early and enhanced support to optimise the development of eligible medicines, speed up their evaluation and contribute to timely patients' access.

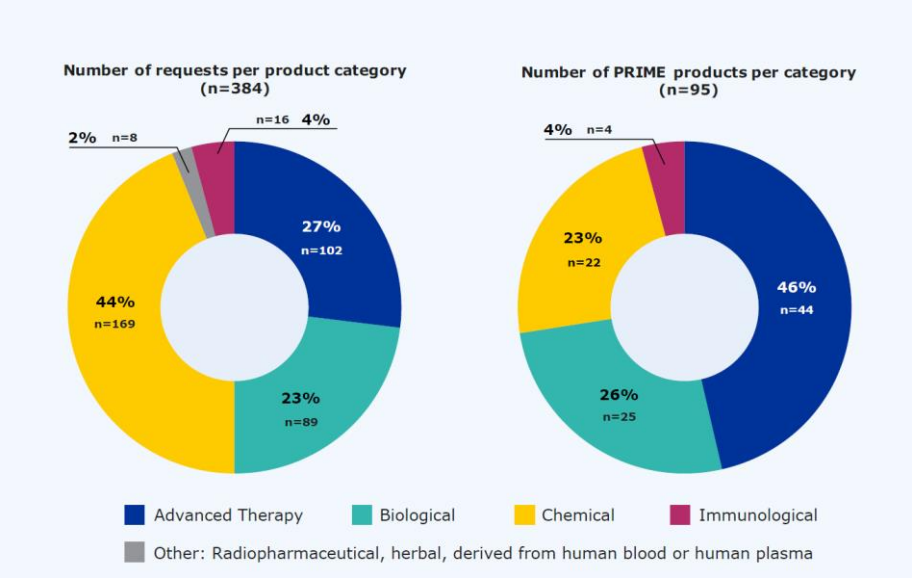
- CAT/CHMP enhanced support for the development of medicines that target an unmet medical need and has potential to be a "game-changer",
- building on existing regulatory tools (SA/PA and accelerated assessment),
- PRIME eligibility based on "proof-of-concept" data,
- early-entry PRIME eligibility, based on "proof-of-principle"/FIH data only, allowed and encouraged for SMEs/Academic developers – to be switched into a full PRIME eligibility,
- early and enhanced dialogue. How?

(https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines, https://www.ema.europa.eu/en/documents/report/prime-analysis-first-5-years experience_en.pdf, https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines#key-figures-12641)

The PRIME as a journey

- The PRIority Medicines (**PRIME**) scheme:

- ATMPs account for approximately 27% of the requests received for PRIME eligibility, they present the highest success rate corresponding to 46% of all PRIME products (7 March 2016 - 30 June 2021). Such rate is confirmed up to now.



(https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines, https://www.ema.europa.eu/en/documents/report/prime-analysis-first-5-years experience_en.pdf, https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines#key-figures-12641)

- CAT statistics

Initial Evaluation of Marketing Authorisation Applications (MAA) for ATMP							
	2009-2021	2022	2023	2024	2025	2026*	Total
Submitted MAAs	35	1	4	7	3	0	51
Positive draft Opinion	20 [i]	6	1	1	4	2	34[#]
Negative draft opinions	4 [i,ii,iii]	0	0	0	3[vii]	0	7
Withdrawals	8 [ii, iv]	1[v]	1[vi]	0	3[viii]	0	13
Ongoing MAAs							4

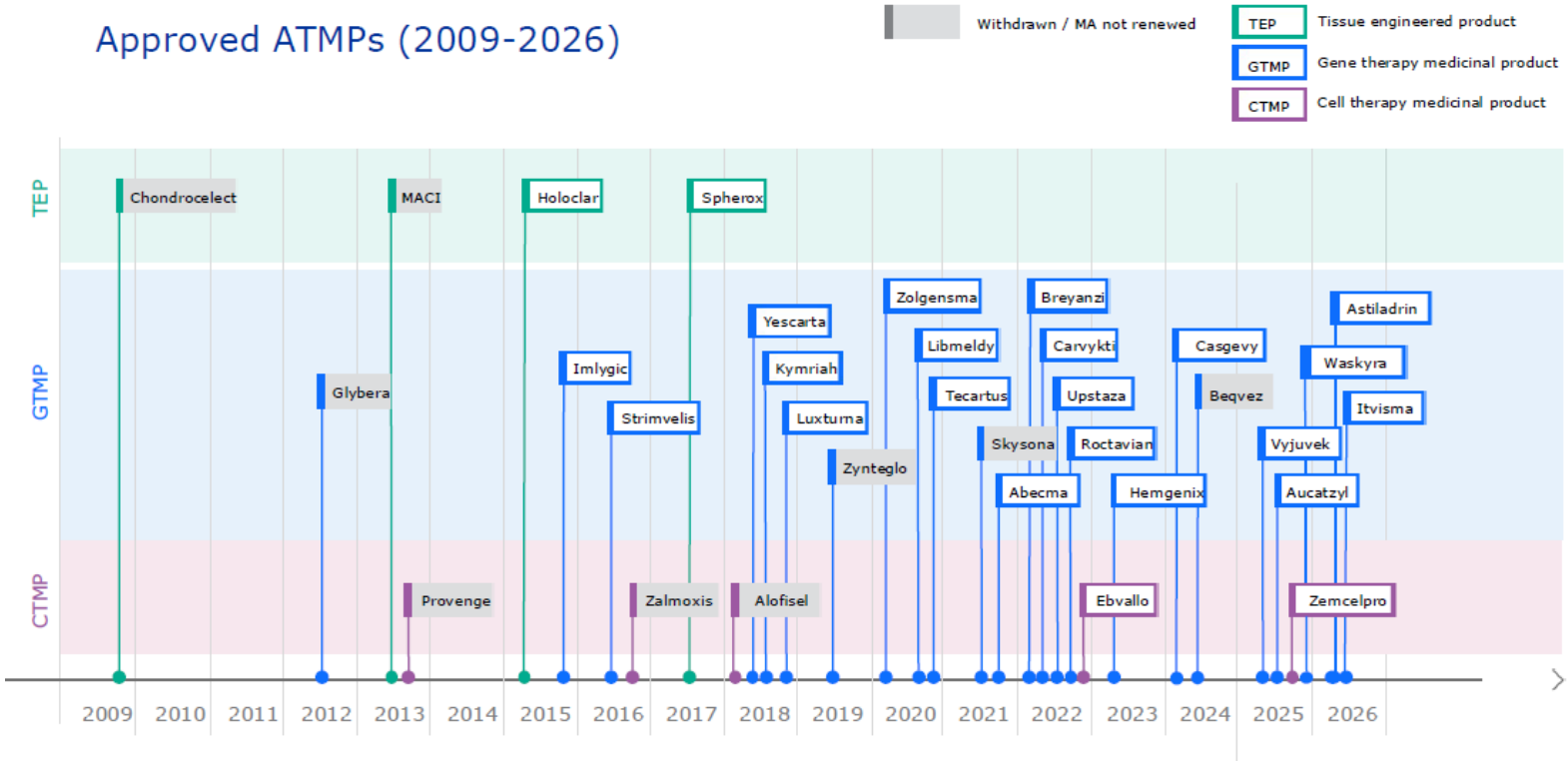
 # Corresponding to 33 ATMPs (see List of authorised ATMPs)
[i] One negative draft opinion and two positive draft opinions for the Glybera
[ii] Negative draft opinion and withdrawal for the Cerepro
[iii] Two negative draft opinions for Heparesc
[iv] Luxceptar, Roctavian, Artobend
[v] Sitoiganap
[vi] Lumevoq
[vii] Elevidys, Jelrix (two negative draft opinions)
[viii] Amtagvi, Fanskya, Jelrix (after re-examination)

PRIME² Eligibility for ATMPs							
	2016-2021	2022	2023	2024	2025	2026*	Total
Discussed	105	10	13	17	21	18	184
Granted	46	4	9	6	6	7	78

* Period: January – May 2026

(https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-june-2026_en.pdf)

- The last 10 years of ATMPs



(https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-june-2026_en.pdf)

- **Classification procedure:**
  - for anybody (SMEs, pharmas, no-profit),
  - 60 days procedure,
  - confirmation of compliance with ATMP definitions,
  - classification outcomes are published.

Scientific recommendation on advanced therapy classification[1]							
	2009-2021	2022	2023	2024	2025	2026*	Total
Submitted	555	51	43	40	28	20	737
Adopted	544	46	52	39	32	14	727

[1] More information on the scientific recommendation on advanced therapy classification and the summaries of ATMP classification can be found on the ATMP classification webpage.
It is stressed that the scientific recommendation on advanced therapy classification does not amount to any endorsement of the plausibility of the product, including the mode of action or therapeutic indication(s) claimed by the applicant.

- **Certification procedure:**
  - for SMEs only,
  - 90 days procedure,
  - pre-evaluation of Q and NC data, any stage of the ATMP development,
  - product development on track for a future MA application,
  - positive evaluation: certificate.

(https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-june-2026_en.pdf)

- **Scientific advice (SA)/protocol assistance (PA):**
  - questions on Q, NC and C development + post-marketing issues,
  - written scientific & regulatory guidance to ATMP developers,
  - 90% fee reduction for SMEs, 65% for others,
  - Protocol assistance free-of-charge to SMEs & academic developers. SA free-of-charge to academic-owned PRIME and ATMP PILOT products. Starting Jan-25, SA free-of-charge to no-profit developers.

Scientific advice procedure for ATMPs						
	2009-2021	**2022**	**2023**	**2024**	**2025**	**2026***	**Total**
Number of procedures	506	53	57	61	76	29	782

- Involvement in **any scientific or regulatory matter/context** requiring expertise in ATMPs including early dialogue platforms fostering innovation (*e.g.*, innovation task force (ITF) meetings, drafting of guidelines, etc).

(https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-june-2026_en.pdf)

- **CAT cluster activities**

- **ATMP cluster teleconference(s)**

- Established: 2008,
- Meeting frequency: every other month,
- Participants: regulators (EMA/CAT – FDA - Health Canada – PMDA- Swissmedic),
- The objective of the cluster is to develop a common understanding of each Agency's regulatory approaches for ATMPs.
- Documents exchanged include scientific advice, ATMP classification reports and assessment reports of marketing-authorisation applications from EMA and Investigational New Drug (IND), pre-IND, and pre-biologics-license-application meeting minutes from the FDA. Both agencies share their (draft) guidelines.

- **Collaboration on gene therapies for (ultra) rare diseases (CoGenT) - the CoGenT pilot EMA-FDA CBER project**

- International regulatory partners participating in internal regulatory meetings and meetings that include the Sponsors,
- Exploring the potential for concurrent submissions and collaborative reviews of gene therapy applications with international regulatory partners (under strict confidentiality agreements),
- Reducing delays, facilitating cross-agency coordination, and expediting reviews,
- Reduce duplication of efforts across borders,
- Accelerating the availability of gene therapies to global patient populations.

(https://www.ema.europa.eu/en/partners-networks/international-activities/cluster-activities)

EMA pilot "Enhanced support to academic developers of ATMPs"

EMA will provide enhanced regulatory support for up to five selected ATMPs that address unmet clinical needs and are developed solely by academic and non-profit developers in Europe.

- Academic developers are a key source of ideas and basic research,
- Aim is to increase the level of translation of basic research into medicines / products,
- Learn how to interact, support and adapt to academic developers,
- Focused regulatory support within the existing regulatory frame,
- Up to *5 academic products*, so far three products selected:

- ARI-0001; Hospital Clinic Barcelona,
- TregTacRes, modified (tacrolimus resistant) T regulatory cells, developed by Berlin Center for Advanced Therapies (BeCAT) as adjunctive therapy after living donor kidney/solid organ transplantation,
- Telethon003, autologous CD34+ cells transfected with a lentiviral vector (containing the human WAS cDNA), developed by Fondazione Telethon (Italy) for Wiskott Aldrich Syndrome.

(https://www.ema.europa.eu/en/news/ema-pilot-offers-enhanced-support-academic-and-non-profit-developers-advanced-therapy-medicinal-products)

Innovation Meeting (IM) – AIFA & EMA (Innovation Task Force (ITF) meetings)

Multidisciplinary platform
for preparatory dialogue and orientation on
innovative methods, technologies and medicines

NCA -> EU- IN (scale to the European network with the Applicant's agreement)

- Support **innovative** drug development
- **Early informal** dialogue with opinion leaders
- 1,5-hour discussion – *Free of charge*
- Brainstorming "style" on innovation in areas without existing guidance
- First step to engage is submit completed 3-page template

(IM @AIFA info here: https://www.aifa.gov.it/innovazione-e-scientific-advice
ITF @EMA info here: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/innovation-task-force-briefing-meetings)

Scientific Advice (SA)/Protocol Assistance (PA) – AIFA & EMA - 1

Advising developers on product-specific questions during development of medicines *to meet regulatory and scientific requirements:*

1	how to manufacture them
2	how to test them in non-clinical studies
3	how to test them in humans in clinical trials
4	how to study them in specific populations (e.g., rare diseases and children)
5	prospective in nature, it is NOT a pre-assessment

Not legally binding

(https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance, https://www.aifa.gov.it/scientific-advice)

Scientific Advice (SA)/Protocol Assistance (PA) – AIFA & EMA - 2

- **National Scientific Advice (NCA):** feedback from AIFA on GMP aspects, suitability of the proposed development plan (Q, NC, C, post-approval measures) to support a national MAA, suitability of the proposed development plan (Q, NC, C) concerning clinical trials to be conducted only in IT.

- **Simultaneous National Scientific Advice** (Coordinating Unit - PEI, AEMPS and FAGG-AFMPS): feedback from the concerned NCAs on the suitability of the proposed development plan (Q, NC, C) concerning clinical trials to be conducted in multiple EU Member states - Accelerating Clinical Trials in the EU (ACT EU Priority Action 7),
  - Pre-CTA advice pilot: feedback from the Member States concerned on pre-CTA submission topics, i.e., technical and regulatory support and not scientific.

- **EMA Scientific Advice (EMA/SAWP):** feedback from the EMA on the suitability of the proposed development plan (Q, NC, C, post-approval measures) to support a centralized MAA.
  - Joint Scientific Consultation: feedback on the suitability of the proposed development plan from EMA (MAAs) and HTA bodies to minimize avoidable divergences,
  - SAWP/CTCG pilot on SA: feedback on the suitability of the proposed development plan from SAWP (MAAs) and CTCG (CTAs) to minimize avoidable divergences.

(https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance, https://www.aifa.gov.it/scientific-advice)

Qualification of Novel Methdologies

Procedure to guide the development of novel, more efficient ways to develop medicinal products (development of new endpoint for clinical trials, new imaging methods, new biomarkers, etc).

Voluntary, scientific pathway for innovative methods or drug development tools not yet integrated in the drug development and clinical management paradigm

Qualification advice

- On future protocols and methods for further development towards qualification
- Evaluation of scientific rationale and preliminary data
- Confidential

100 days

Qualification opinion

- On the acceptability of a specific use of the proposed method in an R&D context
- Assessment of submitted data
- Publicly available

130 days + 60 days public consultation

Examples: methods to predict toxicity, strategies to enrich a patient population for a clinical trial, surrogate clinical endpoints, patient/caregiver reported outcomes, patient registries…

(https://www.ema.europa.eu/en/qualification-novel-methodologies-medicine-development)

Further European & national scientific and regulatory support tools

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 March 2026
EMA/64341/2026

EU-Innovation Network guidance on available scientific and regulatory support tools at national and European level for human medicinal products/technologies/methodologies

(https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/EU-IN/2026_03_EU-IN_guidance_available_scientific_and_regulatory_support_tools_at_national_and__European__level.pdf)

GTMPs - CAR T cell-based medicinal products (anti-CD19 & anti-BCMA, so far)

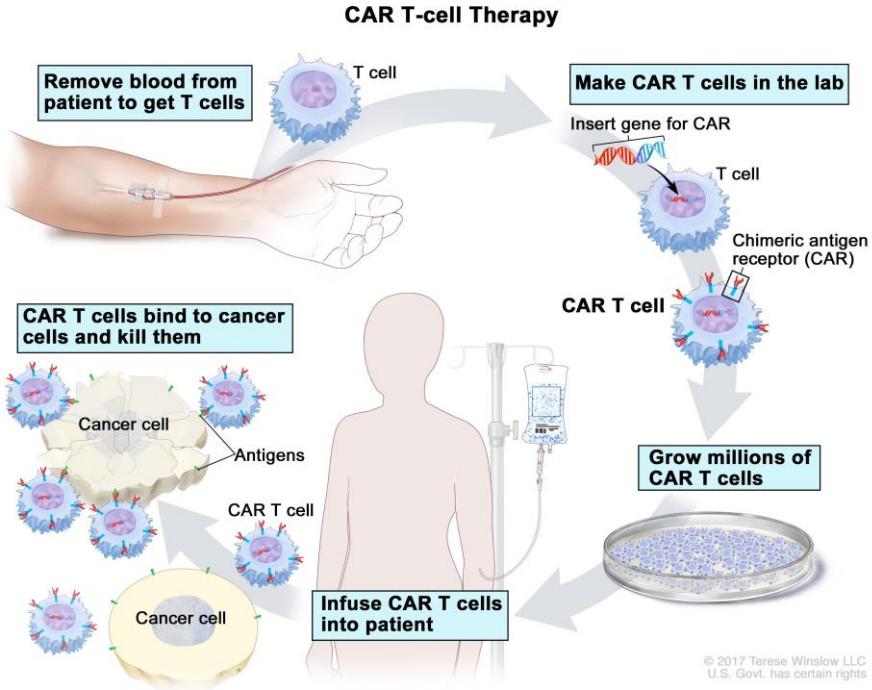
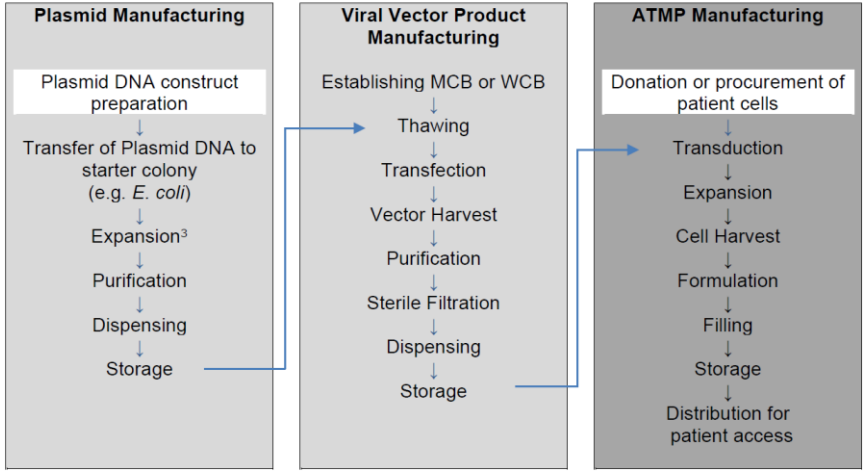


Figure 3: Autologous CAR-T cell therapy ATMP manufacturing



GTMPs - CAR T cell-based medicinal products (anti-CD19 & anti-BCMA, so far)

Breyanzi is indicated for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL), high grade B-cell **lymphoma** (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy.
Breyanzi is indicated for the treatment of adult patients with relapsed or refractory DLBCL, PMBCL and FL3B, after two or more lines of systemic therapy.
Breyanzi is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Abecma is indicated for the treatment of adult patients with relapsed and refractory **multiple myeloma** who have received at least two prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti CD38 antibody and have demonstrated disease progression on the last therapy.

GTMPs – Adeno-associated viral vectors (AAVs)

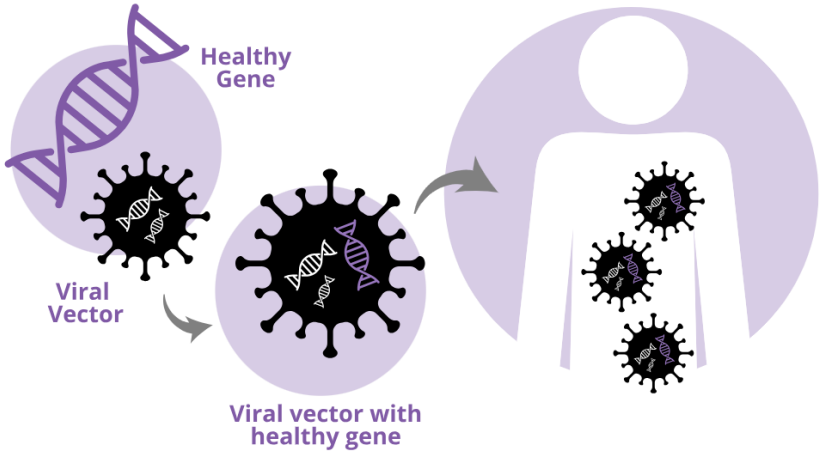
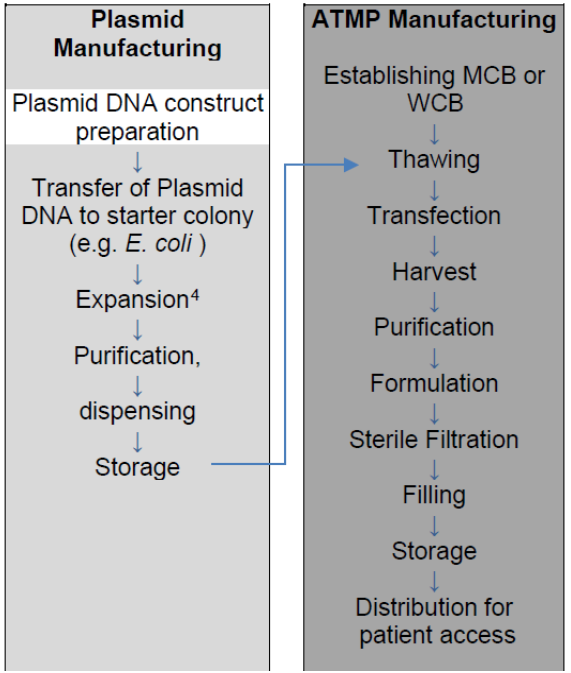


Figure 2: Example of in vivo viral vector gene therapy ATMP manufacturing



GTMPs – Adeno-associated viral vectors (AAVs)

Roctavian is indicated for the treatment of severe **haemophilia A** (congenital factor VIII deficiency) in adult patients without a history of factor VIII inhibitors and without detectable antibodies to adeno-associated virus serotype 5 (AAV5).

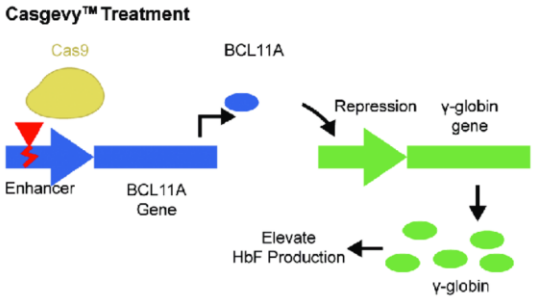
Zolgensma is indicated for the treatment of:
patients with 5q **spinal muscular atrophy (SMA)** with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or
patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

GTMPs – CRISPR gene editing-based products

casgevy®
(exagamglogene autotemcel)
suspension for IV infusion

Casgevy is indicated for the treatment of transfusion dependent **β thalassemia** (TDT) in patients 12 years of age and older for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA) matched related HSC donor is not available.

Casgevy is indicated for the treatment of severe **sickle cell disease** (SCD) in patients 12 years of age and older with recurrent vaso occlusive crises (VOCs) for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA) matched related HSC donor is not available.



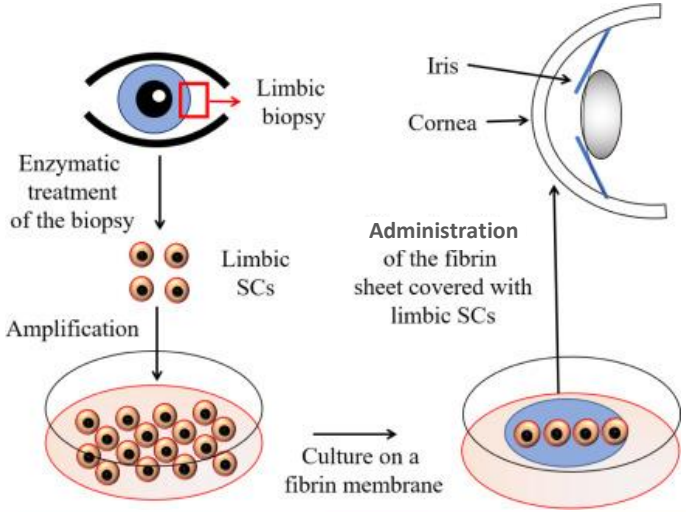
Casgevy aims to **upregulate γ-globin expression**, thereby increasing the production of fetal hemoglobin (HbF) as a therapeutic strategy for sickle cell disease and β-thalassemia.

The treatment functions by **disrupting an erythroid-specific enhancer region** of the BCL11A gene, a transcriptional repressor of γ-globin. Inhibition of BCL11A leads to derepression of the γ-globin gene, **resulting in elevated HbF levels**, which can functionally compensate for deficient or abnormal β-globin in affected individuals.

TEPs – Tissue engineered product

HOLOCLAR®
Ex vivo expanded autologous human corneal epithelial cells containing stem cells

Holoclar is indicated for the treatment of adult patients with moderate to severe **limbal stem cell deficiency** (defined by the presence of superficial corneal neovascularisation in at least two corneal quadrants, with central corneal involvement, and severely impaired visual acuity), unilateral or bilateral, due to physical or chemical ocular burns. A minimum of 1-2 mm2 of undamaged limbus is required for biopsy.



спасибо
谢谢
GRACIAS
THANK YOU
ありがとうございました
MERCI
DANKE
धन्यवाद
شُكراً
OBRIGADO

Barbara Bonamassa, PhD

Italian Medicines Agency (AIFA)

Innovation and Pharmaceutical Strategy Department

Via del Tritone, 181

00187 Rome – Italy

e-mail: b.bonamassa@aifa.gov.it