EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Advanced therapy medicinal products (ATMPs) and ATMP Regulation

RD-ACTION, European Medicines Agency, and European Commission-DG SANTE workshop: how European Reference Networks can add value to clinical research

Presented by Patrick Celis on 29 May 2018
CAT Secretariat

Content

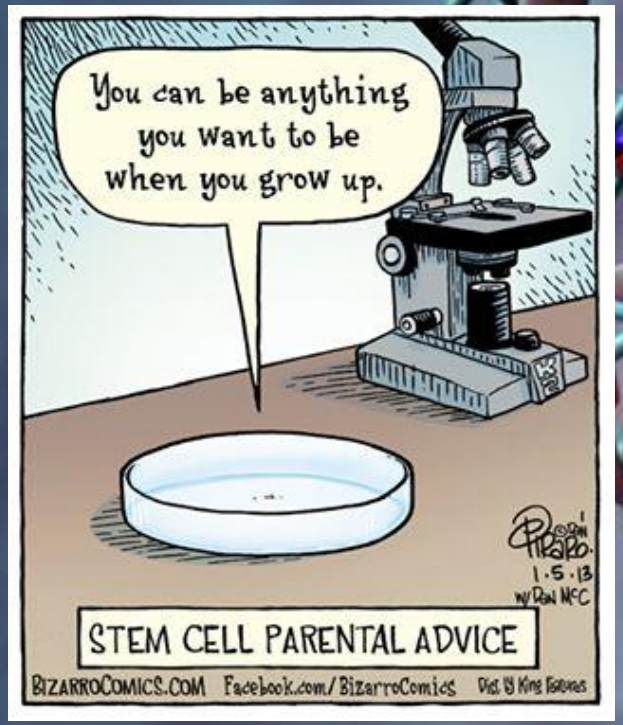
- Advanced therapy medicinal products (ATMPs): what are they? why are they so different from other medicines?

- Why is there a special legislation for ATMPs? The European regulatory framework

- Support to ATMP developers – EMA support to innovation.

The ~~Beauty~~ and the ~~Beast~~

Genes **Cells**



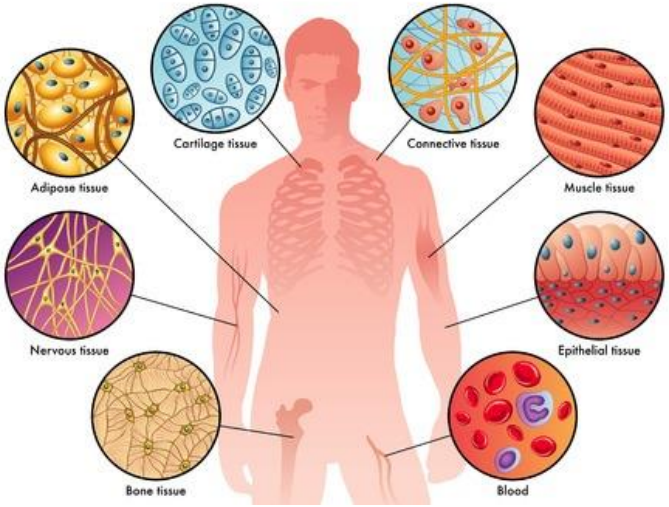
ATMPs:

- Gene therapy medicinal products
- Somatic cell therapy medicinal products
- Tissue engineered products

Credit: Christoph Bock/Max Planck Institute for Informatics

Pinterest.com

Gene therapy medicinal products



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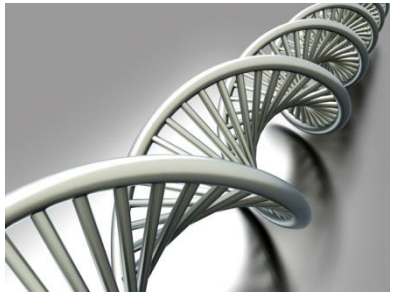


DNA/RNA

- Treatment of inherited disease
  - Glybera
  - Strimvelis
- Cancer therapies
  - Imlygic
- Tissue regeneration (e.g. loss of sight)
  - Zalmoxis

Somatic cell therapy medicinal product – tissue engineered product

Alofisel

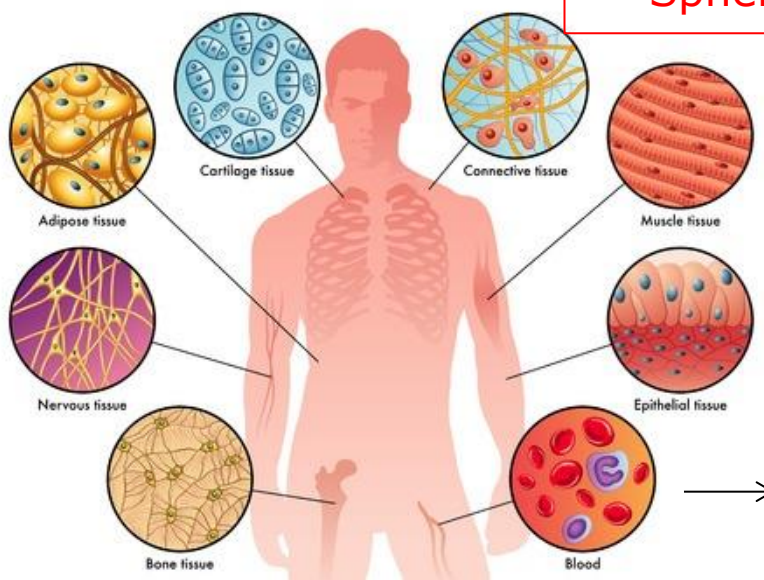
Products against immune diseases, …

Treatment of Parkinson's disease, Alzheimers, ALS

Holoclar

Treatment of cartilage defects

Chondrocelect
MACI
Spherox



Product for cardiac repair

Skin replacement

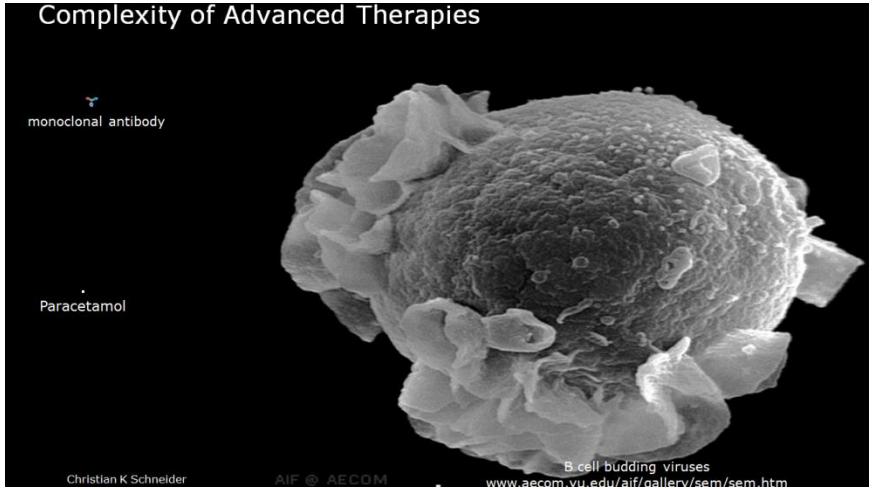
Cancer Immunotherapy

Provenge

Pinterest.com

ATMPs are …

- Medicinal products based on cells or genes
- Very different from medicines based on chemical entities or biological / biotechnological origin

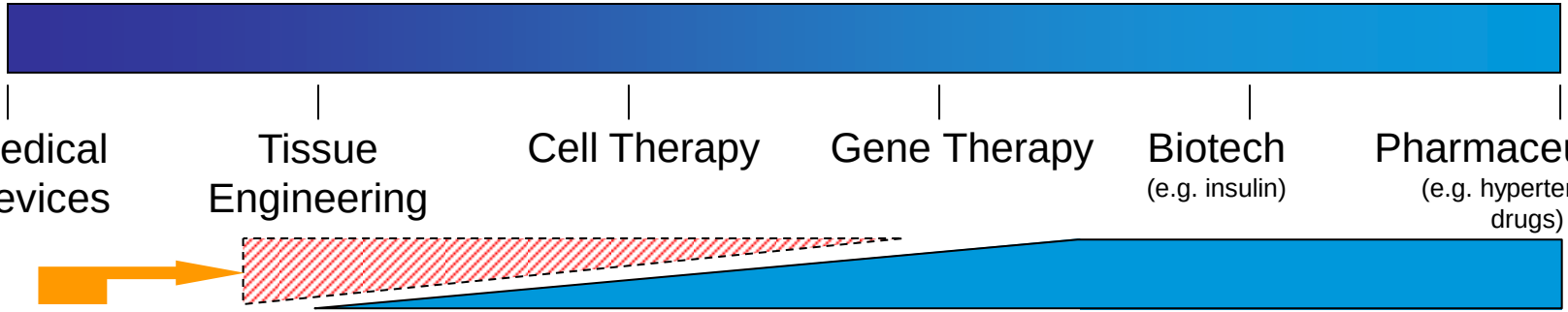


- But same requirement for testing / controlling each batch
  - Impact on cost of manufacture of the ATMPs
  - Very small batch size (autologous CBMP: batch size = 1)

Legislation

Science

Advanced Therapies



ATMPs and the EU legal framework – Lex specialis

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

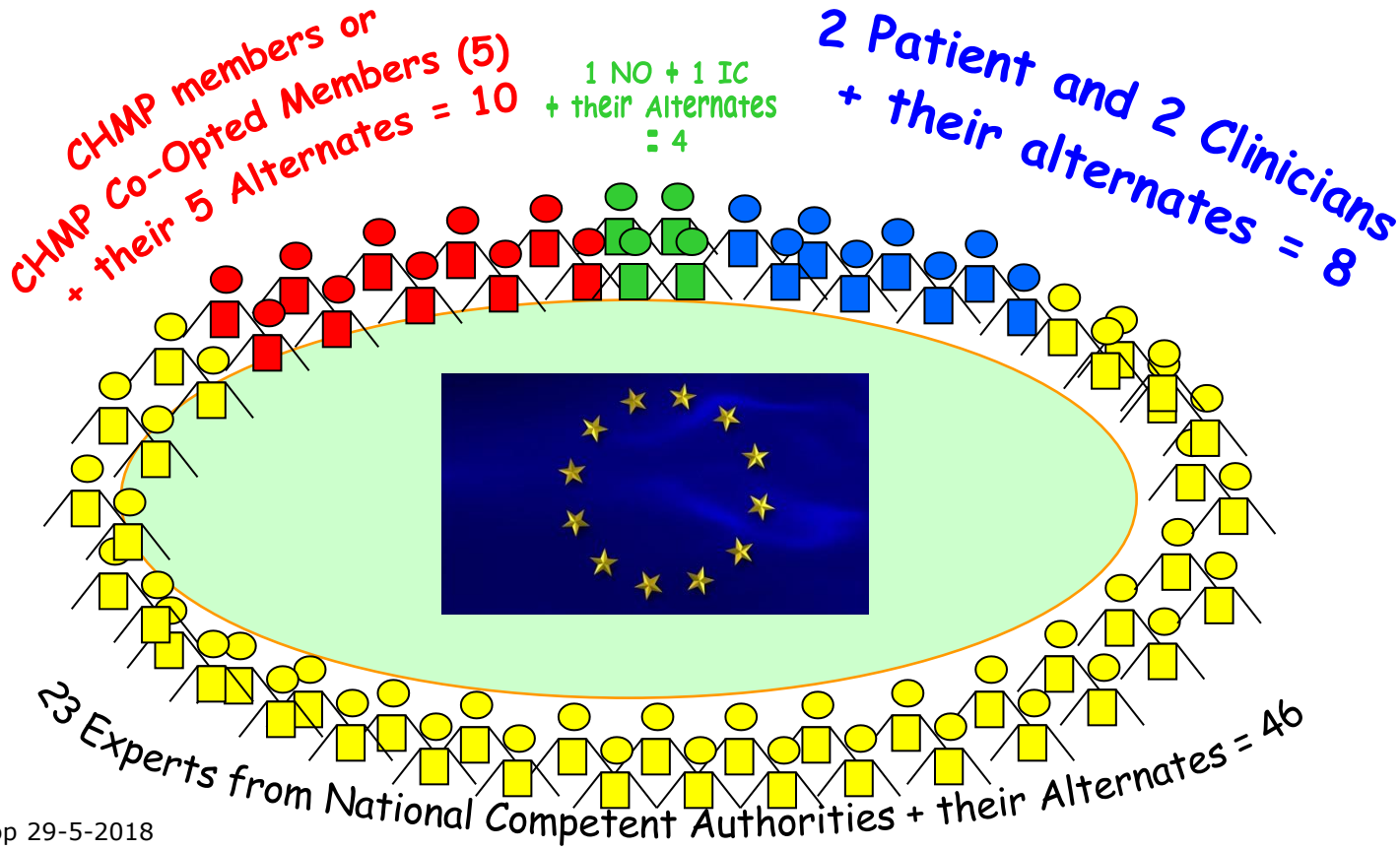
on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004

(Text with EEA relevance)

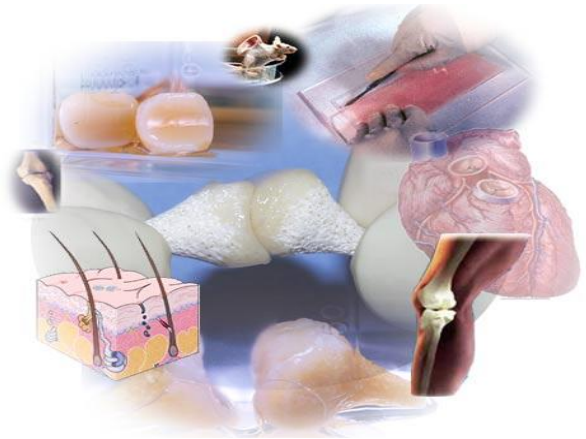
Some highlights of the ATMP Regulation (1397/2007)

- ATMPs
  - Definitions
  - ATMPs are medicinal products
  - ATMPs are authorised in the EU via the centralised procedure
- Principles of existing legislation on medicines apply to advanced therapies:
  - marketing authorisation
  - demonstration of Quality, Safety & Efficacy
  - GMP, GCP (adapted to ATMPs)
  - post-authorisation vigilance and RMP
- Sets up a specialist Committee, the Committee for Advanced Therapies (CAT)

Committee for Advanced Therapies



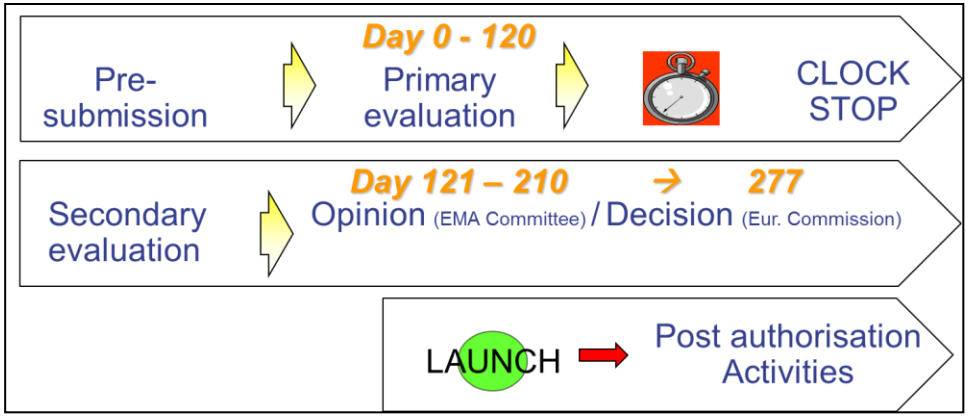
Tasks of the Committee for Advanced Therapies (CAT)



- EVALUATION
- CERTIFICATION
- CLASSIFICATION
- Scientific Advice
- Support to PDCO
- Support to CHMP / COMP
- Interaction with stakeholders
- Publications, Guidelines

Marketing Authorisation of ATMPs

- Centralised MA: one license valid in entire EU
- 210-day procedure
- Review by CAT
- Final opinion adopted by CHMP



Incentives in the ATMP Regulation

- Scientific Advice:
  - Questions on Quality, Non-clinical and Clinical development + Post-marketing studies
  - Aim: provide scientific certainty to ATMP developers
  - 90% fee reduction for SMEs, 65% for others

- Scientific recommendation on advanced therapy classification
  - 'Is the product I am developing an ATMP?

- SMEs: Certification of quality and non-clinical data
  - 'Is my product development so far on track for a future Marketing Authorisation Application?'

ATMP classification: what is it?

- Simple procedure, incentive included in the ATMP Regulation
  - 60 day procedure (often shorter), no fee
- To provide regulatory certainty to the ATMP developers:
  - 'Am I developing an ATMP?' (what legislation do I have to consult)
  - 'What guidelines are applicable to my product?'
- For early developments (no expectation that the product is already in non-clinical or clinical development)

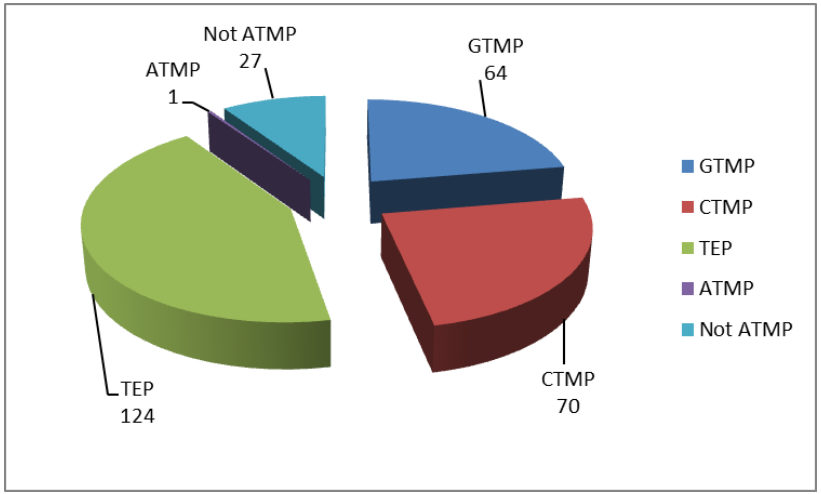
Classification procedure for ATMPs

- All classification outcomes are published (summary)

http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/04/WC500126681.pdf

- Up to end April 2018:
  - 298 procedures finalised
  - 307 procedures submitted

Finalised classifications



(Status Dec 2017)

ATMP Certification procedure

- Incentive: early-late
- For SMEs only
- Scientific certainty
  - 'Is my product development so far on track for a future Marketing Authorisation Application?'
- CAT will perform a scientific evaluation of
  - (early) quality / development data
  - (early) non-clinical data

ATMP Certification procedure

- 90 day procedure
- The applicant will always received the evaluation report and List of issue for future consideration
  - If positive evaluation: Certificate by EMA
- 10 Certification procedures finalised
  - 1 withdrawn because ‘too early’ (Q-certification)
  - In recent cases: pre-assessment of Q/NC data, shortly before MAA.

ATMPs in Europe (May 2018)

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over 500 clinical trials using ATMPs in EU

298 ATMP classifications

293 scientific advice requests

20 MAAs reviewed / Under review

10 ATMPs approved

3 withdrawn
1 Suspended

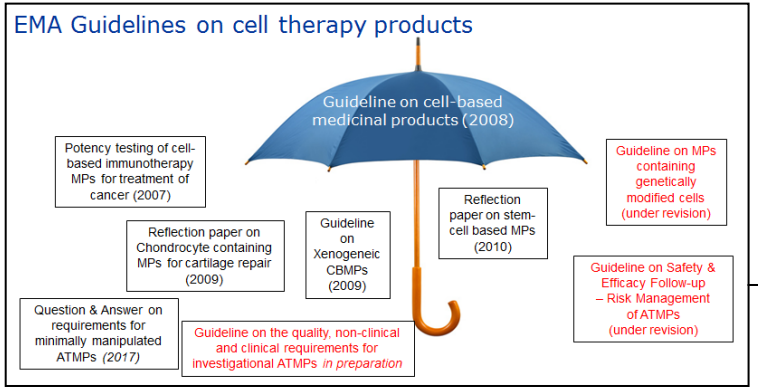
Market

6 licensed ATMPs

EMA support to innovation

- Support to all developers
  - Scientific guidelines
  - Scientific advice
  - EU Innovation network and ITF meetings
  - SME
- Specific incentives for ATMP developers
  - ATMP classification
  - ATMP certification
- Early access mechanism
  - Conditional MA and Accelerated Assessment
  - PRIME

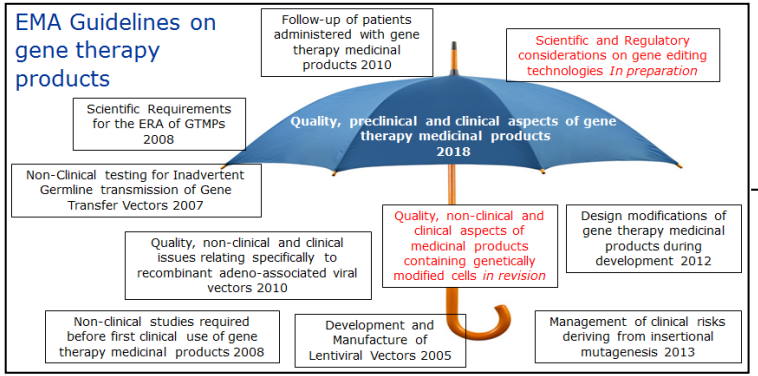
Guidelines for gene and cell-based medicinal products



Visit the EMA website: www.ema.europa

Human regulatory ▸ Research and development ▸ Scientific guidelines ▸ Multidisciplinary

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000405.jsp&mid=WC0b01ac058002958a



http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000410.jsp&mid=WC0b01ac058002958d

Early support

- EMA's Innovation Task Force
  - Discussion platform for early dialogue with applicants (SMEs, academia, researchers)
  - ITF Briefing meetings with EMA staff, with involvement of members of Committees/Working Parties
  - Discussion of regulatory and scientific issues

- EU Innovation Network
  - Regulatory support to medicines innovation and early development of new medicines
  - Collaborative effort of EMA and EU national competent authorities

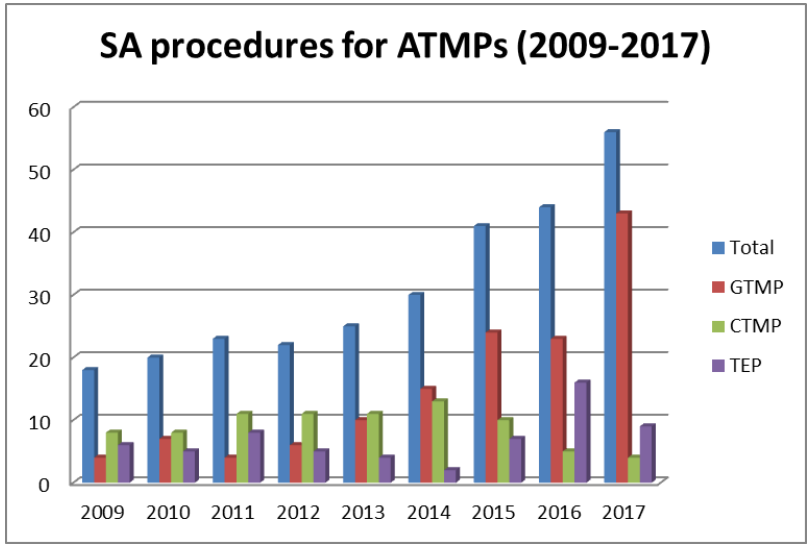
Scientific Advice (more to come)

Incentive: early – late / scientific certainty

- Open to all applicants
  - Fee reduction for SMEs
  - Fee reduction for ATMP developers (non-SMEs)
  - Protocol assistance (reduced fee) for Orphan medicinal products
- Scientific advice is given from the SAWP of the CHMP in collaboration with the CAT (+ other committees & working parties)
- Simple, fast procedure: 40 or 70 days (if face to face meeting with the Applicant)
- Possibility for parallel SA with FDA / parallel SA with HTA

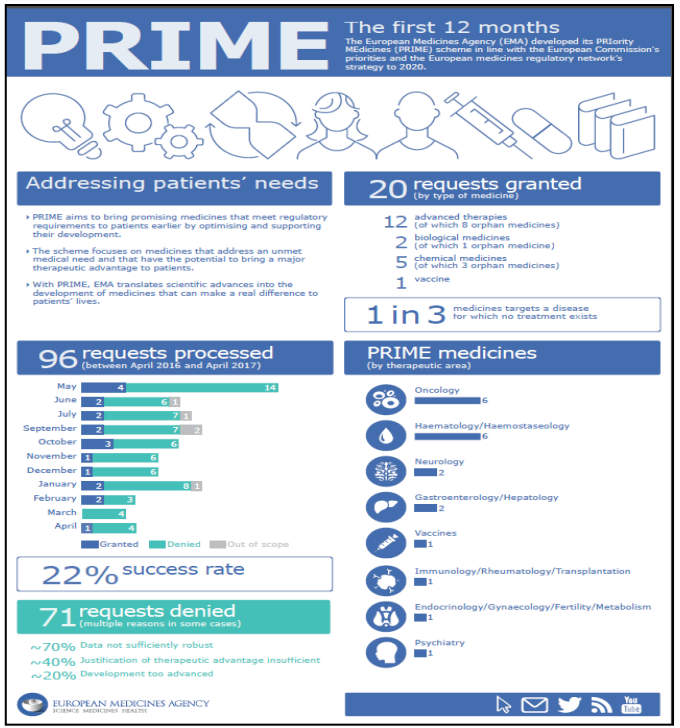
Scientific Advice for ATMPs

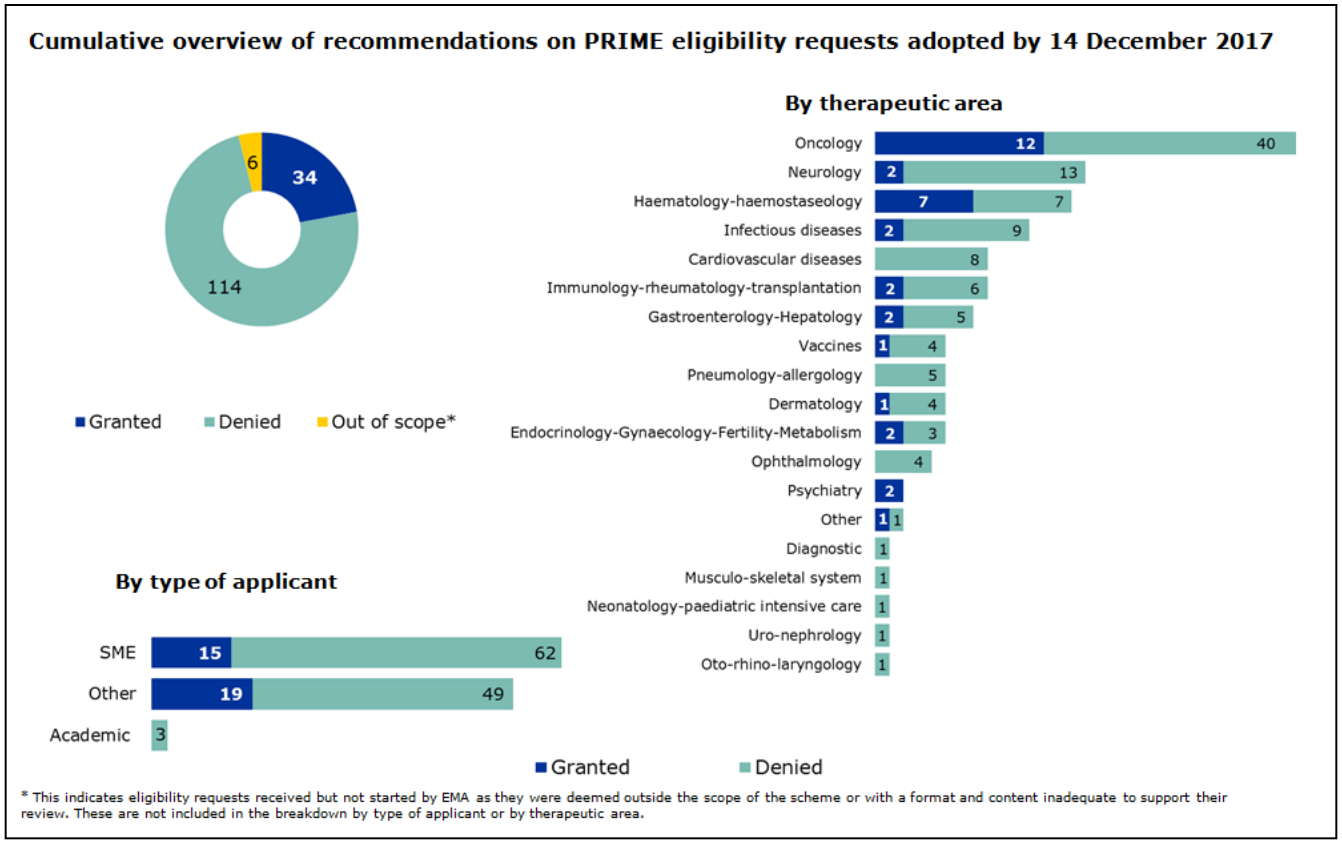
- 293 SA procedures started (April 2018) – CAT routinely involved in all SA for ATMPs
- Increase in SA's for ATMPs over period 2012 – 2017
- Majority of SA nowadays for GTMP (76% in 2017)



Scientific Advice (SA) requests until end of 2017

How we support innovative medicines: PRIME Scheme





Out of the 34 PRIME granted, 14 were for ATMPs (41%):
- 13 are GTMPs, 1 CTMP
- 8 Oncology, 4 Haematology, 1 Transplantation, 1 Neurology

European Commission-DG Health and Food Safety and European Medicines Agency Action Plan on ATMPs

The term "advanced therapy medicinal products" ("ATMPs") is used to designate gene therapies, somatic cell therapies and tissue engineered products.

In the EU, these products are governed by Regulation 1394/2007 on advanced therapy medicinal products ("ATMP Regulation"). The cornerstone of the Regulation is that a marketing authorisation must be obtained prior to the marketing of ATMPs. The evaluation of these products is led by a specialised committee within the European

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/10/WC500237029.pdf

Action plan on ATMPs - background

- Multi-stakeholder workshop at EMA on 27 May 2016 to explore solutions to identified challenges to ATMP development and patient access
- **Stakeholders** from Academia, Industry (SME and Big Pharma), Pharmacists, treating physicians, patient representatives, consortia, incubators, investors, Health technology assessment (HTA) bodies, EU Regulators and EC
- **Action plan** is a direct response to the identified solutions
- proposal for actions by **EMA** in close collaboration with **National Competent Authorities** and the **European Commission**
- **Priority:** actions according to feed-back received from stakeholders and actions that can be started in 2017
- Actions that would require changes in the **legal framework of ATMPs** are **not included**
- Additional suggestions and proposals can be re-visited in the future, and included to the plan, as required

Take home messages

- **EMA's key principles**: based on a regulatory network, collective decision making, transparency, supporting innovation.
- **The centralised procedure**: one application leading to one marketing a in all EU member states and the EEA, one invented name & one common product information (available in all languages). Compulsory for ATMPs.
- A clear **regulatory framework for ATMP**: Gene therapy, cell therapy and tissue engineered products approved
- **Early access tools and strong support for ATMPs**: scientific advice, PRIME, ATMP certification/classification, accelerated assessment, conditional marketing authorisation, marketing authorisation under exceptional circumstances.
- **Engaging with EMA**: pipeline meetings, innovation task force, SME office, pre-submission meetings. Early engagement encouraged for ATMPs.

Thank you for your attention

Any questions?

Further information

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