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How CAT Works: Regulatory Process, Patient Contribution and Outcomes

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EURORDIS MEMBERSHIP MEETING
Brussels , 23 May 2012

Outline

1. **Implementation of the Advanced Therapy Regulation at the European Medicine Agency (EMA):**
   - Committee for Advanced Therapies (CAT)
   - Regulatory Centralised Procedures for Advanced Therapy Medicinal Products (ATMPs)
2. **Role of Patients in the CAT**
3. **Outcomes**
4. **Conclusions**

Disclaimer:

These slides are not representative of the official view of the EMA or CAT, but only of their author

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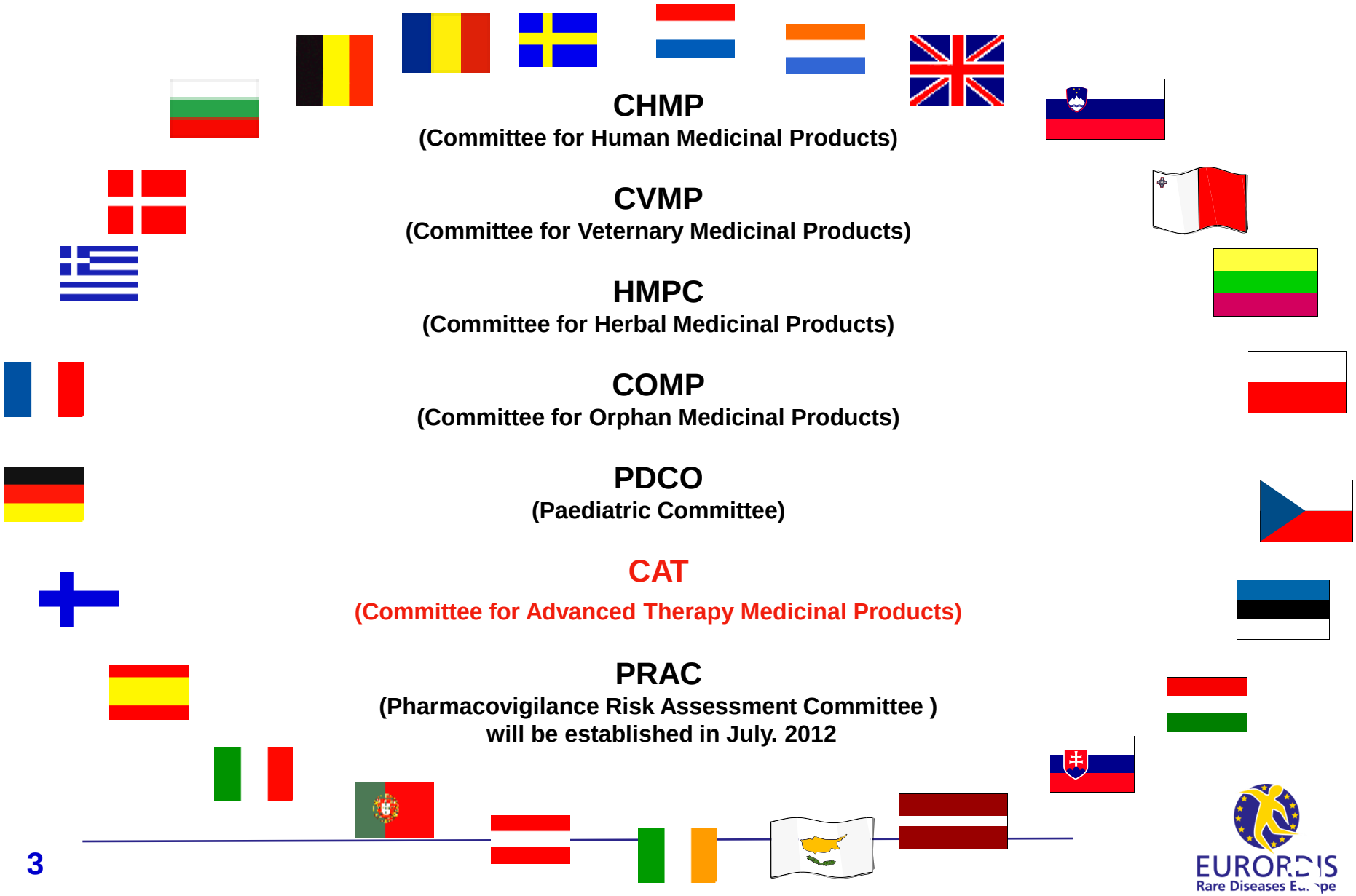
EMA Scientific Committees: ALL EU MEMBER STATES ARE REPRESENTED



CHMP
(Committee for Human Medicinal Products)

CVMP
(Committee for Veternary Medicinal Products)

HMPC
(Committee for Herbal Medicinal Products)

COMP
(Committee for Orphan Medicinal Products)

PDCO
(Paediatric Committee)

CAT
(Committee for Advanced Therapy Medicinal Products)

PRAC
(Pharmacovigilance Risk Assessment Committee)
will be established in July. 2012

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EU LEGAL FRAMEWORK

A complete lack of harmonisation exists across Europe, policy makers adopted in 2007 the Regulation on ATMPs 1394/2007

Other EU legislations that apply to ATMP products:

- **Directive 2001/83/EC** (medicinal products for human use)
- **Regulation (EC) No 726/2004** (procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency)
- **Directive 2001/20/EC** (clinical trials)
- **Directive 2005/28/EC** (good clinical practice, manufacture and import)
- **Directive 2003/94/EC** (good manufacturing practice)
- **Regulation (EC) No 1901/2006** (paediatric medicines)

….And for Rare Diseases….Regulation (EC) 141/2000 on Orphan Drugs

Regulation on Advanced Therapies
Key elements

- **Advanced Therapy medicinal products (ATMP)**
  - **Gene Therapy Products**

  Medicinal product aiming at the transfer of a functional gene into humans
  - **Somatic Cell Therapy Products**

  Medicinal product based on the administration of « sufficiently » manipulated cells into humans
  - **Tissue Engineered Products**

  Medicinal product consisting in engineered cells/tissues administered to human to regenerate, repair or replace a human tissue.
- **Principles of existing legislation on medicines apply to advanced therapies:**
  - **Quality, Safety & Efficacy**
  - **Marketing authorisation**
  - **Post-authorisation vigilance**

Centralised Procedure for ATMPs

- 1 application to EMA → 1 scientific evaluation

- Scientific Committee:
  CAT + adoption by the CHMP

- Maximum legal time limit
  210 days evaluation (CAT Opinion + CHMP Opinion) + EU Commission Decision

- 1 Marketing Authorisation valid for the whole EU

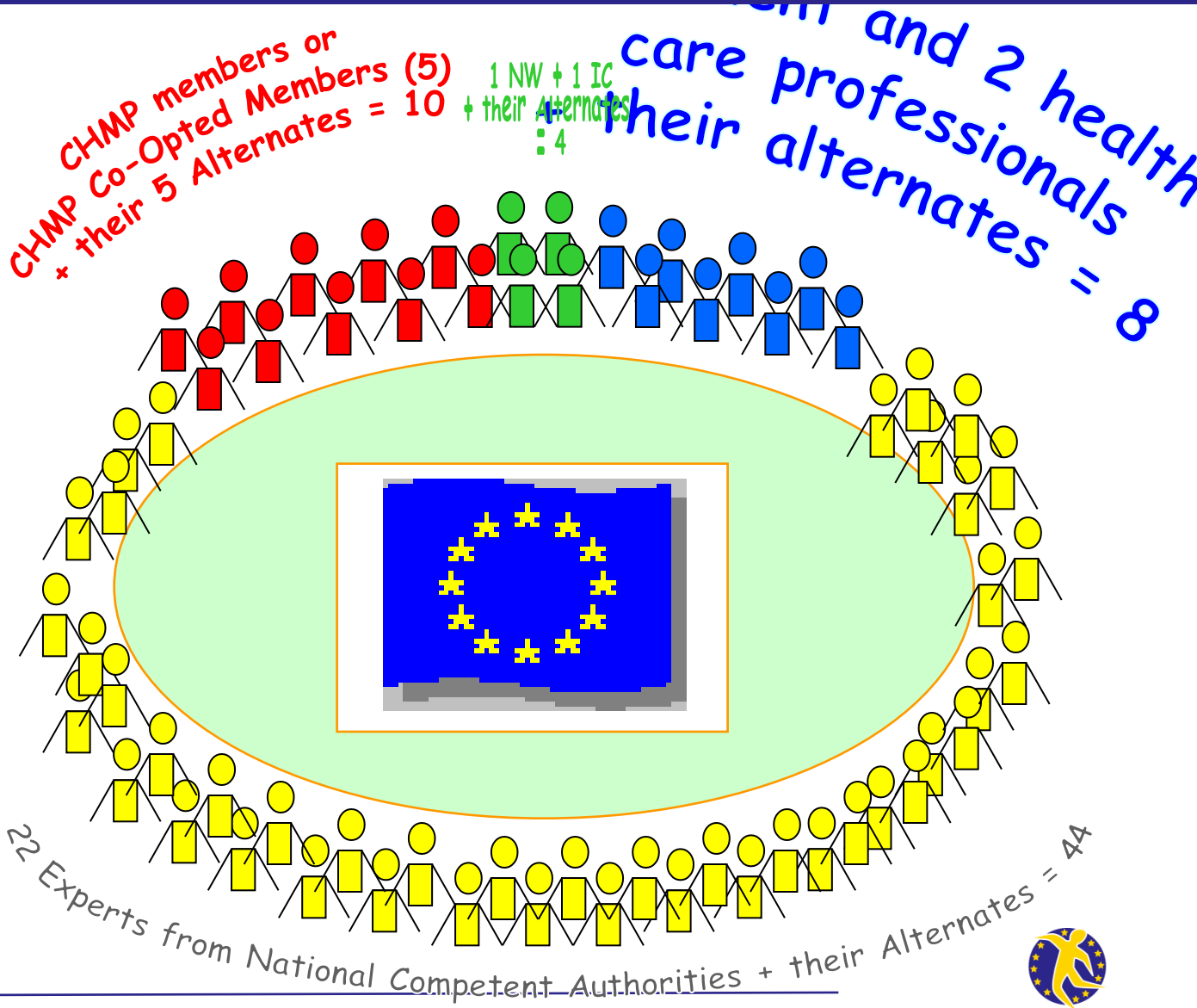
- 1 Trade name and 1 Labelling (all EU languages)
  Summary of Product Characteristics
  User Package Leaflet
  Package Labelling

The Committee for Advances Therapies (CAT): Composition

CAT should cover the scientific areas relevant to advanced therapies, including:

- **Medical devices**
- **Tissue engineering,**
- **Gene therapy,**
- **Cell therapy,**
- **Biotechnology,**
- **Surgery,**
- **Pharmacovigilance,**
- **Risk management**
- **Ethics.**

[Recital 9 & Art.21]



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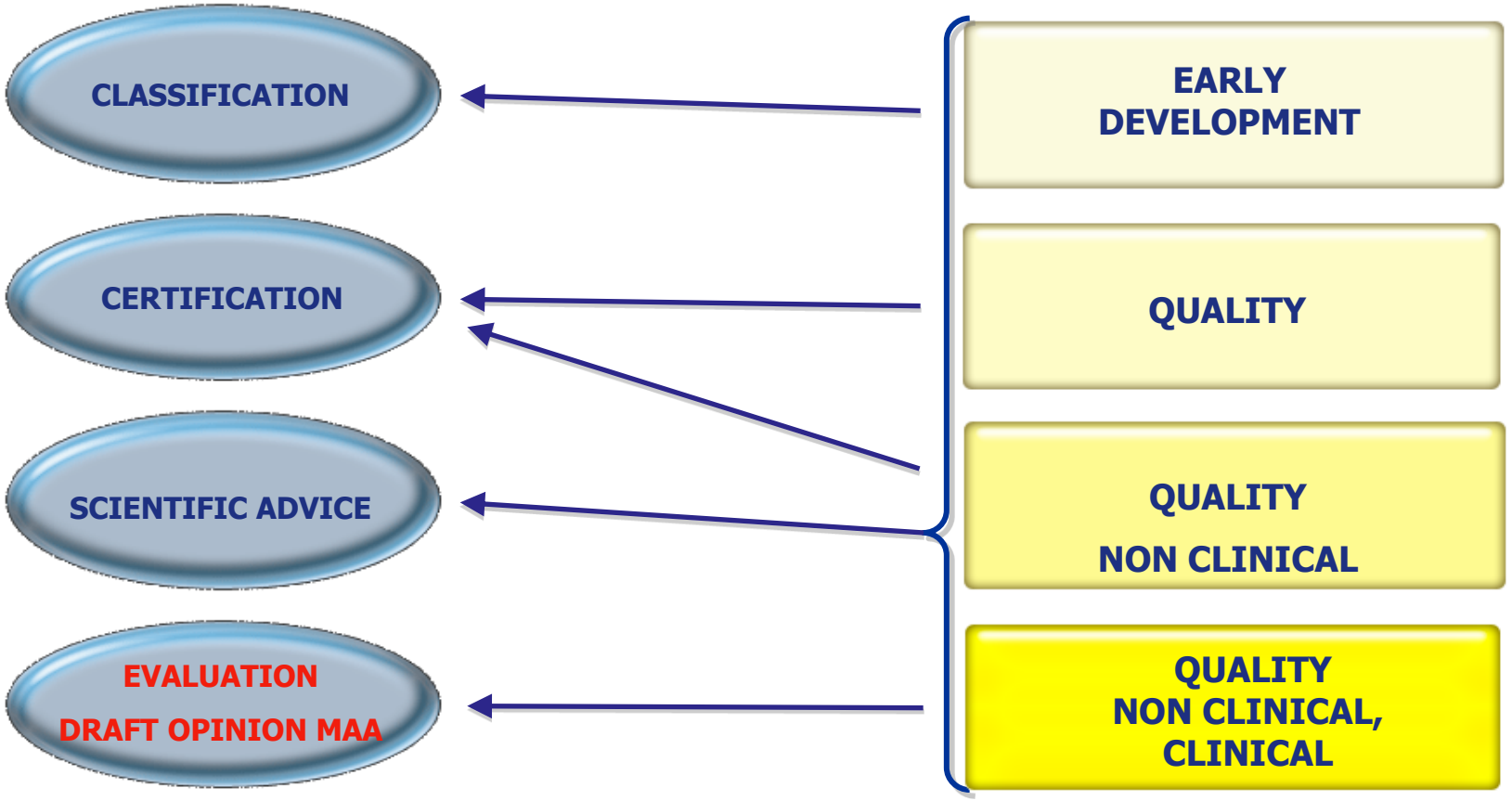
ROLE OF CAT



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EMA Scientific Committees and Patients' Contribution

- **Expertise:** convey a combination of specific education, training and professional experience (not as directly affected person).
- **Experience**: convey practical disease knowledge obtained from direct contact with the disease (affected person or close contact with affected person, e.g. family, carer).
- **Advocacy**: act on behalf of the affected patients in defence of their rights; provide patient-oriented public health / healthcare policy perspective.
- **Empowerment:** Access to the information necessary to participate in the decision-making processes on behalf of all patients.

Role of Patients representatives in the EU Centralized Procedures for ATMP

- **Full members of the CAT**
  - Vote on products / procedures
  - Stand for chair/vice-chair of CAT
  - Can be Rapporteur, Co-Rapporteur, Peer reviewer
  - Can take part of assessment team for:
    - MAA for ATMP
    - Re-registration of products legally on the market
    - Certification of Quality/Non-Clinical data
  - Can be Rapporteur for scientific guidelines

Role of Pos representatives in the EU Centralized Procedures for ATMP

- Representing patients' voice
- Propose patients experts
- Bringing points of view and perspectives on Regulatory procedure
- Link outside POs useful for their specific expertise
- Points of view and real life experience of concerned patients
- Address issues that could concern lay peoples
- Involvement in all the Regulatory process including issues of post-marketing access.
- Propose actions beyond the regulatory framework: e.g. proposal for a CAT work programme addressing general issues related to ATMPs development

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CAT - OUTCOMES

Initial Evaluation of MAA for ATMP	2009	2010	2011	2012	Total
Submitted	3	1	2	1	7
Positive draft Opinion	1	0	1[i]	0	2
Negative draft Opinion	1*	0	1	0	2
Withdrawals	1	1	0	0	2

* Application subsequently withdrawn
[i] Re-examination opinion (Glybera)

Scientific advice procedures on ATMPs	2009	2010	2011	2012	Total
Discussed*	25	30	36	2	**93**
Written comments to SAWP	17	15	8	0	40

CAT: where we are now

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 June 2010
EMA/CAT/235374/2010
Patient Health Protection

Committee for Advanced Therapies (CAT)
Work Programme 2010 - 2015

Introduction – Problem statement

New and emerging science has been identified as an important driver for progress and change in the European Medicine Agency's (EMA) Road Map to 2015[1].

It is generally well recognised in the international scientific arena and by regulators that advanced therapies are at the forefront of scientific innovation in medicine, offering potential groundbreaking new treatments for diseases and injuries of the human body.

The continuous scientific progress, for example in the field of cellular and molecular biology, has boosted the hope for highly innovative and improved therapies and has led in the last decade to intensive research and development in the field of gene therapy and regenerative medicine (including tissue engineering and somatic cell therapy). However, whilst science has revealed the potential, only

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CAT Objectives for the 2010-2015

- **Facilitate development ATMP and access to MAA: understand trends in research and development, strengthen dialogue with stakeholders, reinforce internal/external cooperation**
- **Promote the use of available regulatory procedures and introduce potential improvements**
- **Explore possibilities offered by the current regulatory framework when applied to ATMPs**
- **Contribute to foster innovation**

Conclusions

- ✓ ATMP Regulation implemented
- ✓ Clear framework for MAA
- ✓ Proactive approach to address the needs of the sector
- ✓ Tools to facilitate Translation are available

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Questions ?

Thanks for your attention

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Definitions: GENE THERAPHY

"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;

(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."

Definitions: SOMATIC CELL THERAPHY & TEP

sCTMP and TEP are both containing or consisting of engineered cells or tissues (insert X-ref to definition). To be considered 'engineered' cell or tissue should fulfil at least one of the following criteria:

- substantial manipulation: during the manufacturing process the cell or tissue have been manipulated so that their biological characteristics, physiological functions or structural properties have been modified to achieve their intended function. Example of substantial manipulation: cell selection and expansion, genetic modified cells, etc.

  It should be stressed that the substantial manipulation of the cell and tissue is viewed in light of its link to the effect exerted by the product.

- non-homologous use: the cells or tissues are not intended to be used for the same essential function or functions in the recipient as in the donor. A relevant example is represented by autologous bone-marrow derived cells which are minimally manipulated (e.g. bone-marrow aspirate) injected in the patient's heart for regeneration of the myocardium.

The main difference between the two categories of products is determined on the basis of the intended function of the product. In fact sCTMP are intended for the treatment of diseases whereas TEPs are used in or administered with a view to regenerating, repairing or replacing a human tissue.

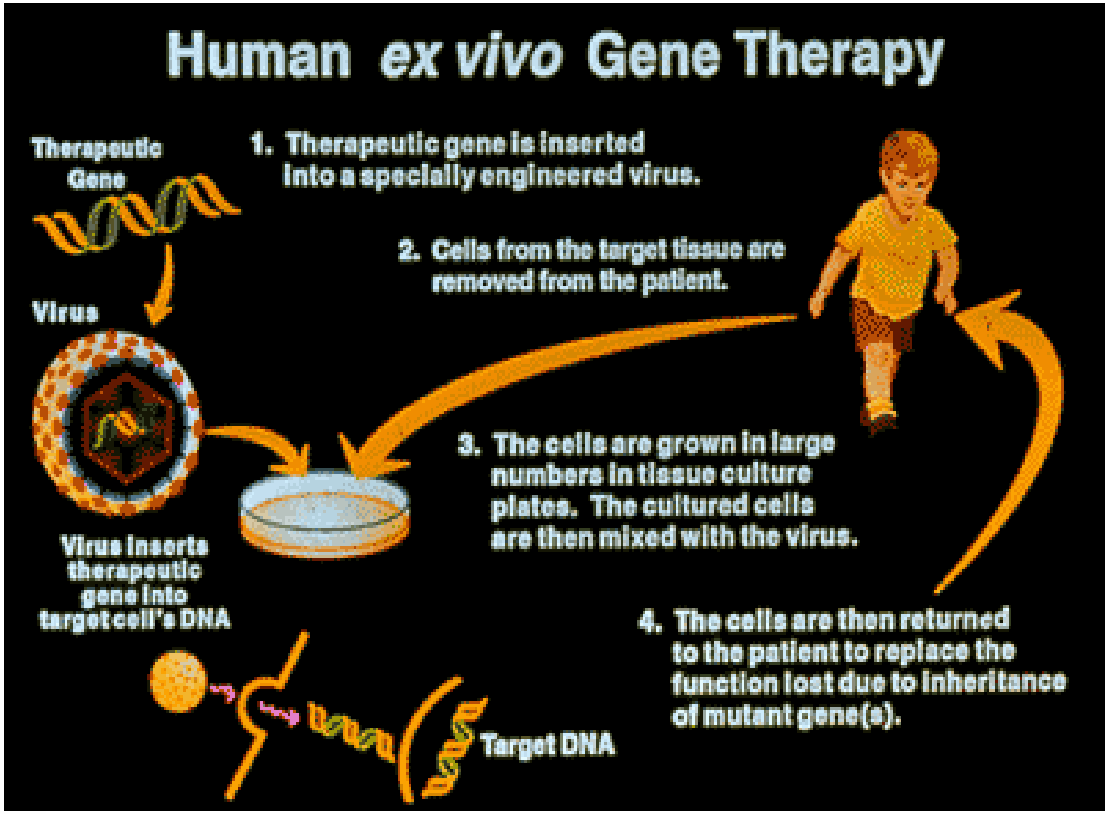
Definitions: COMBINED ATMP

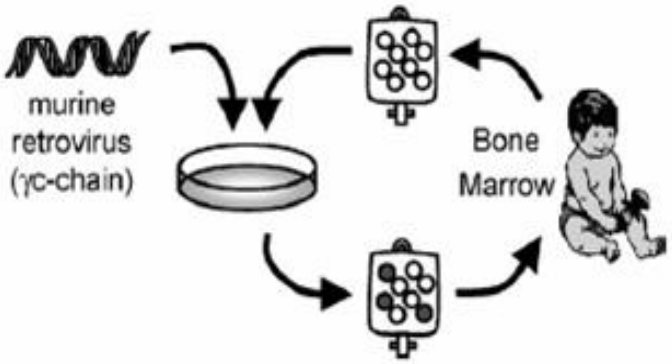
- *it must incorporate, as an integral part of the product, one or more medical devices within the meaning of Article 1(2)(a) of Directive 93/42/EEC or one or more active implantable medical devices within the meaning of Article 1(2)(c) of Directive 90/385/EEC, and*
- *its cellular or tissue part must contain viable cells or tissues,*

or

- *its cellular or tissue part containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to.*

Ex vivo Gene therapy: treatment of SCID disease





http://history.nih.gov/exhibits/genetics/sect4.htm

http://athena.bioc.uvic.ca

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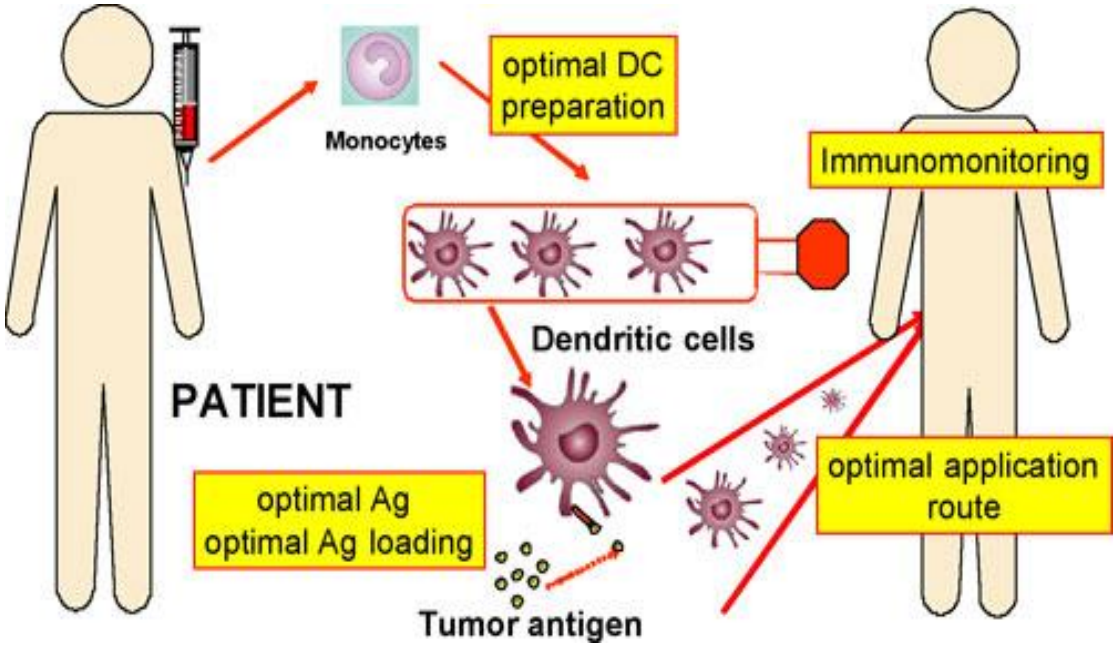
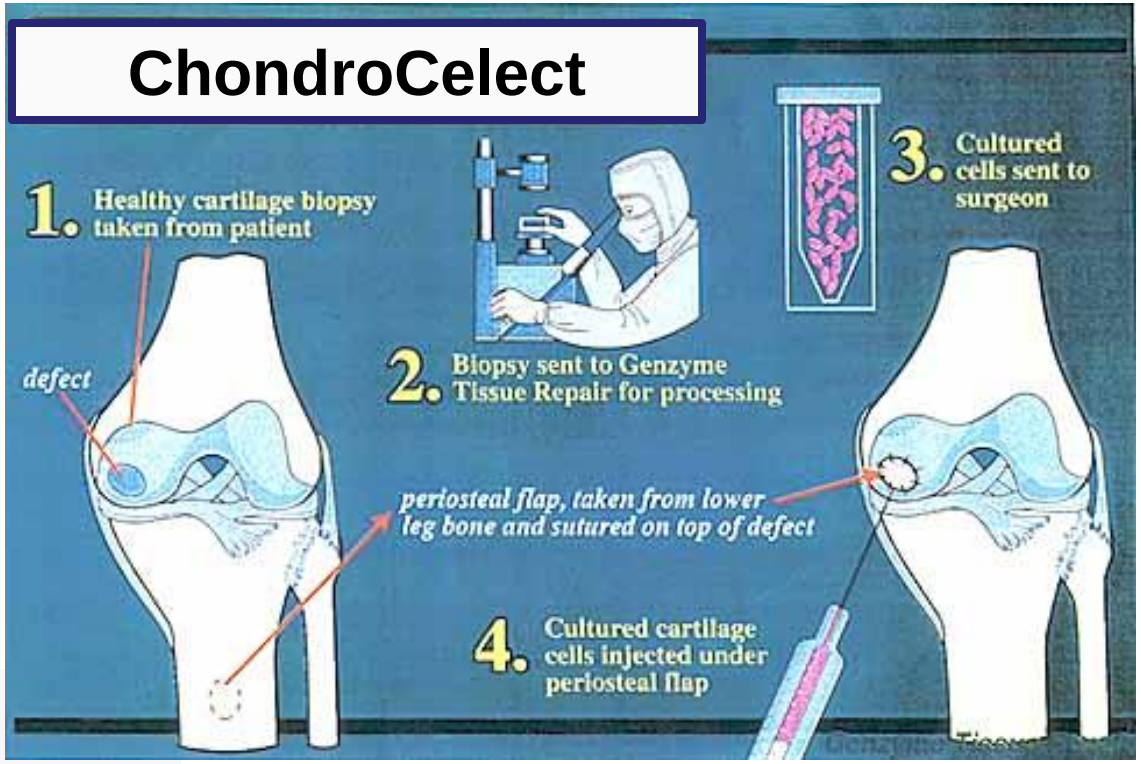
Example: Cancer Cell therapy



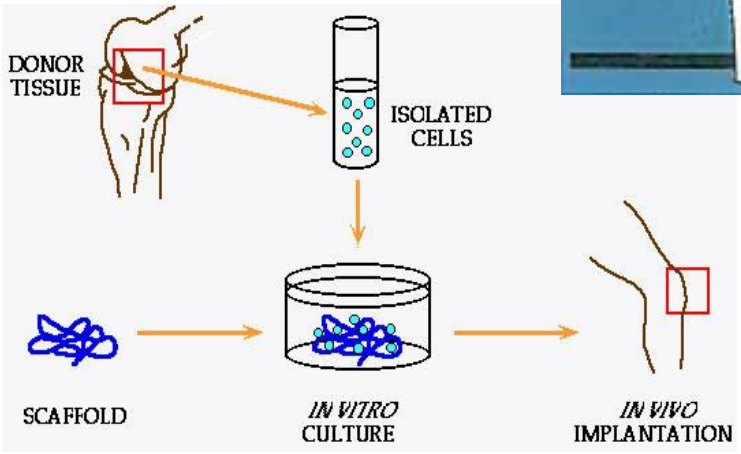
Example: Cartilage repair

First generation →



Second generation

↓



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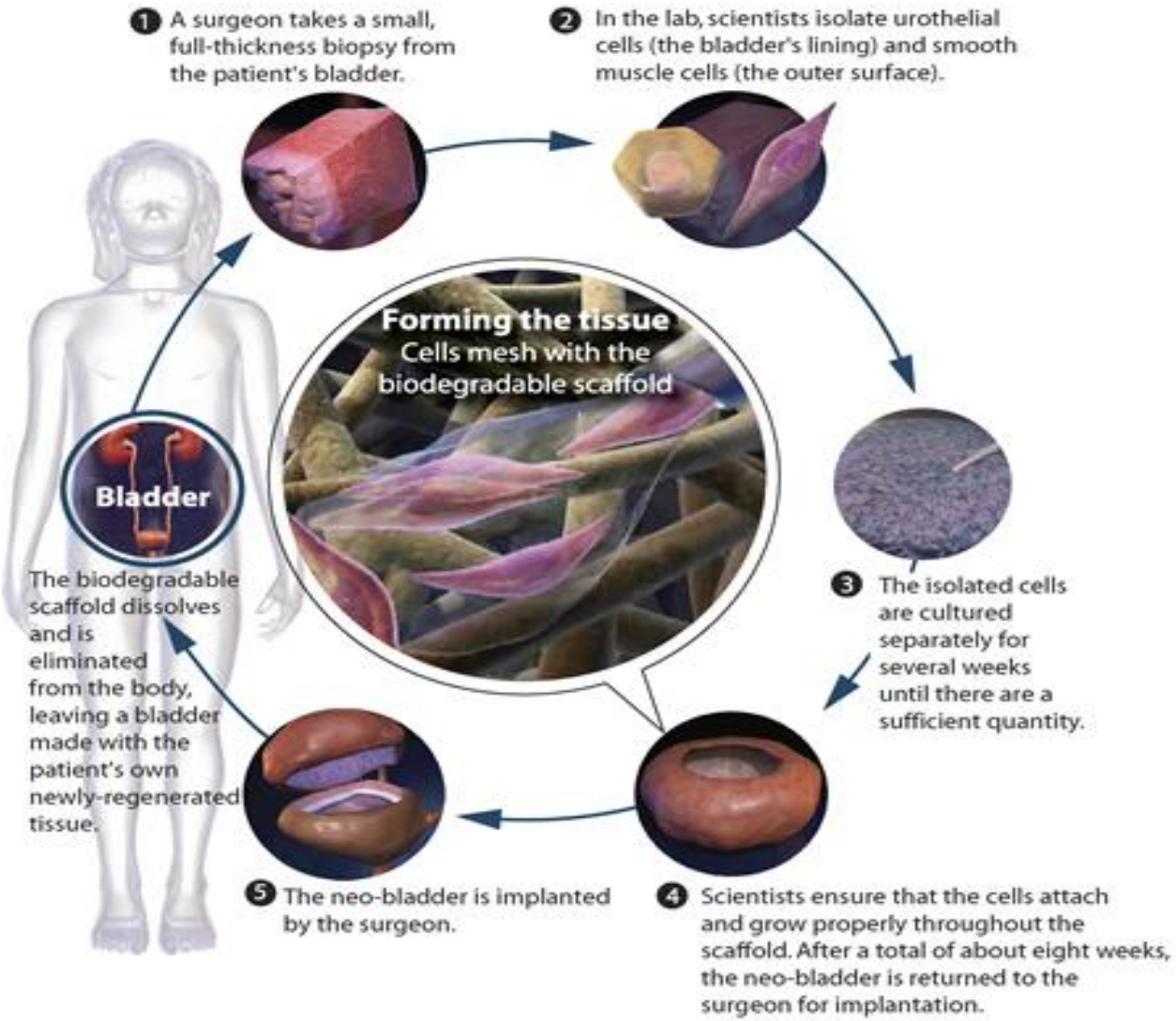
Engineering an Organ

Regenerative medicine technology has the potential to create a functional neo-organ using the patient's own cells to augment or replace a failing organ, for example a bladder.



EMA

- **The EMA** is the European Union body **responsible** for coordinating the existing scientific resources put at its disposal by the 27 EU Member States **for the evaluation, supervision and pharmacovigilance of medicinal products.**

- **Mission Statement** – **"to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health."**