New Regulation for Advanced Therapies including Oncology Biological Products

iSBTc Global Regulatory Summit

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European Medicines Agency (EMEA)

Presentation Overview

- EMEA and the European network
- Centralised authorisation procedure
  - Additional regulatory tools
- Regulation on Advanced Therapies
- Concluding remarks

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The EMEA

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  London E14 4HB
  United Kingdom

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- Fax: +44 (0) 20 7418 8416

- www.emea.europa.eu

Overview of EMEA

- EUROPEAN MEDICINES AGENCY (EMEA)**:**
  REGULATION (EC) No 726/2004

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

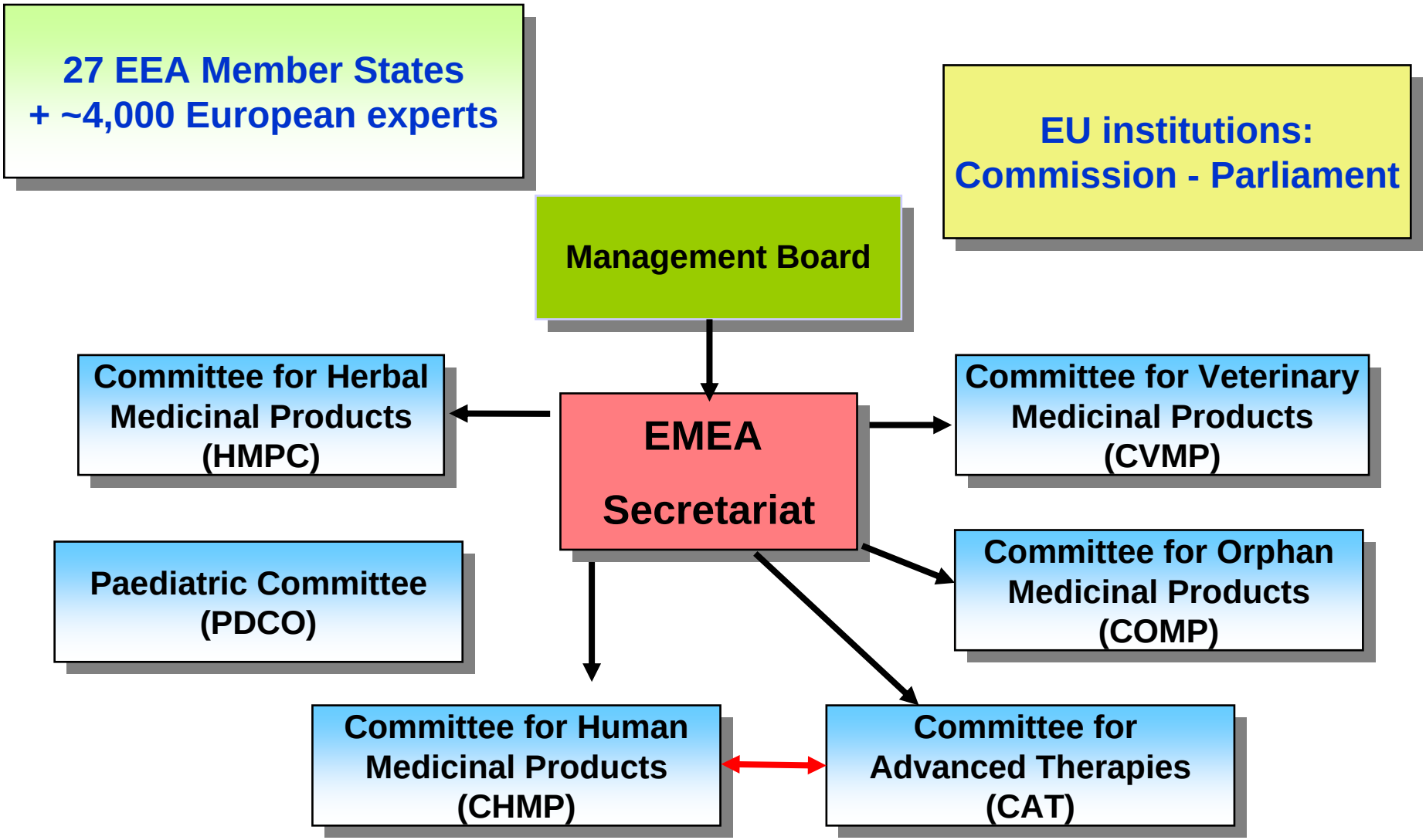
- Responsible for the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use.

Evolution of the EU Network

- EMEA Established 1993
- Centralised procedure
  - European Marketing Authorisation
- Expansion – 27 Member States

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

EMEA Organisation and Partners



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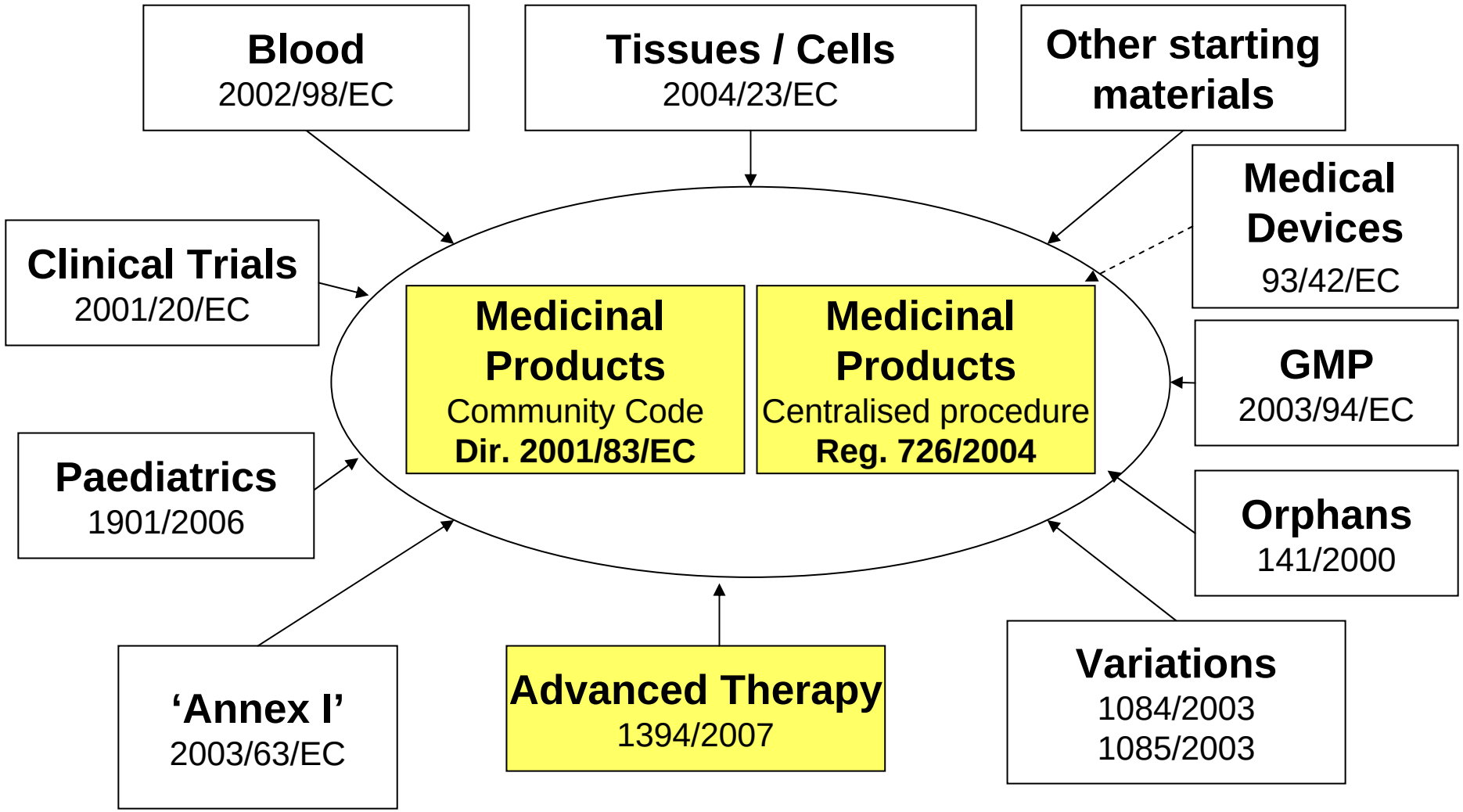
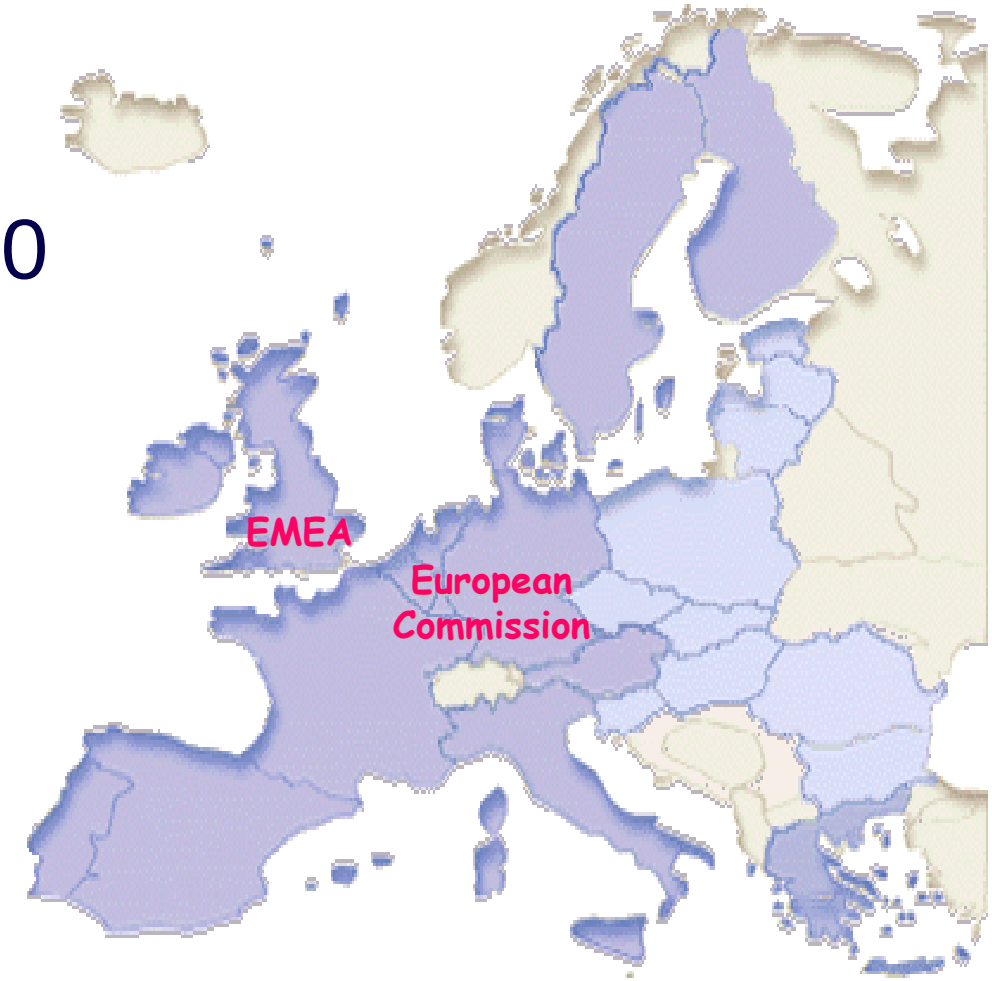
EU regulatory framework



Centralised Procedure

- Rapid (277 days = 210 days for evaluation, 67 days for authorisation)

- EU-wide Marketing authorisation (license)



Centralised procedure

- **1 Assessment**
- **Scientific Committee:**
  - CHMP - Committee for Medicinal Products for Human Use
  - CAT – Committee for Advanced Therapies
- **Maximum time limit**
  210 days evaluation to CHMP Opinion → Decision (MA)
- **1 Marketing Authorisation** valid whole EU
- **1 Invented name**
- **1 Common Labelling** (all EU languages identical)
  Summary of Product Characteristics
  User Package Leaflet & Package Labelling

Centralised procedure

- Scope (mandatory)
  - Biotechnology products / ATMP
  - Orphan drugs
  - Medicines for treatment of:
    - AIDS, Cancer, Neurdegenerative disorders, Diabetes, auto-immune diseases/immune disfunctions, Viral diseases
- Scope (optional)
  - New chemical entity
  - Significant therapeutic, scientific or technical innovation

Centralised Procedure - TIMETABLE

Day 0 - 120

Pre-submission → Primary evaluation →  CLOCK STOP

Day 121 – 210 - 277

Secondary evaluation → Opinion/ Decision

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LAUNCH → Post authorisation Activities

New regulatory tools – Conditional marketing authorisation

- **Authorisation** valid for 1 year**, renewable**
- **Allows for** increased flexibility **when granting a MA**
- **Conditions:** unmet medical need **and benefit to public health of** immediate availability **overweighs risks inherent that additional data is required.**
- **Limited to medicinal products:**
  - Aimed at preventing, treating or for medical diagnosis of **seriously debilitating or life-threatening diseases**,
  - **Emergency threats** (WHO, EC)
  - **Orphan** medicinal products

New regulatory tools – Accelerated review

- Accelerated review
  - **150 days** instead of 210 days
    - Possibility to revert back to normal timetable during the procedure
  - For products with **major public health interest – therapeutic innovation**

Clinical trial applications

- In EU, authorisation of clinical trials remain the responsibility of the member states where the trial in conducted
- Harmonised procedure (based on same legislation) and requirements for clinical trial applications
- EMEA is hosting the ‘Clinical trials coordination group’
  - Discussion on common principles and processes to be applied throughout the European medicines regulatory network

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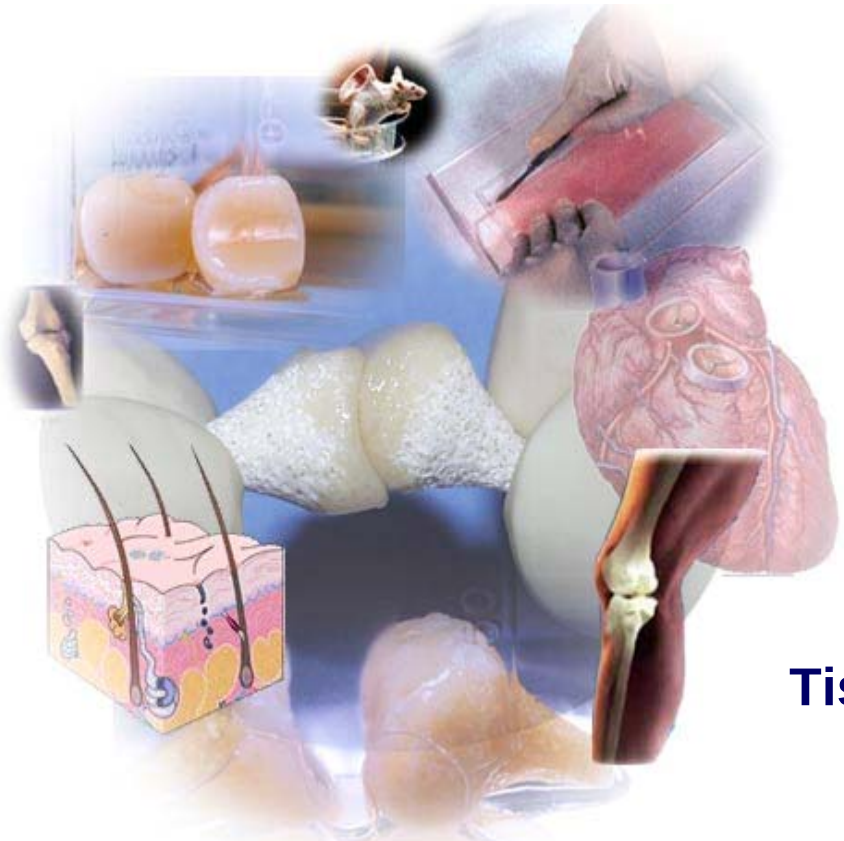
Advanced Therapy Medicinal Products
ATMP

Regulation (EC)
No 1394/2007

Effective
30 December 2008



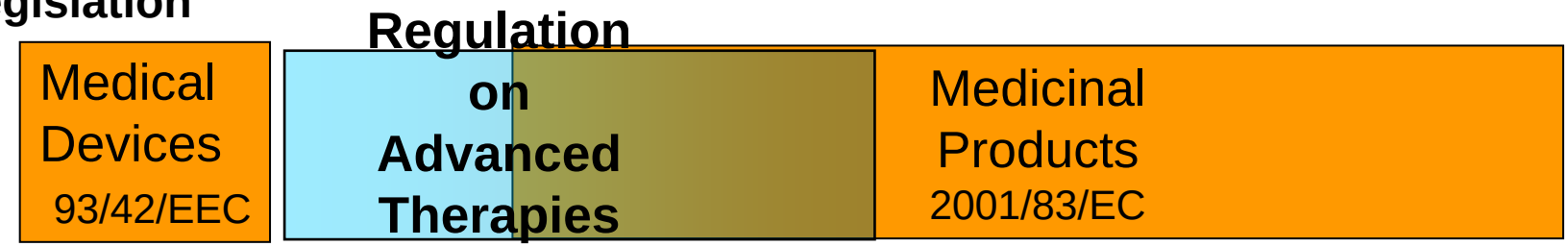
Cell Products

Gene Therapy

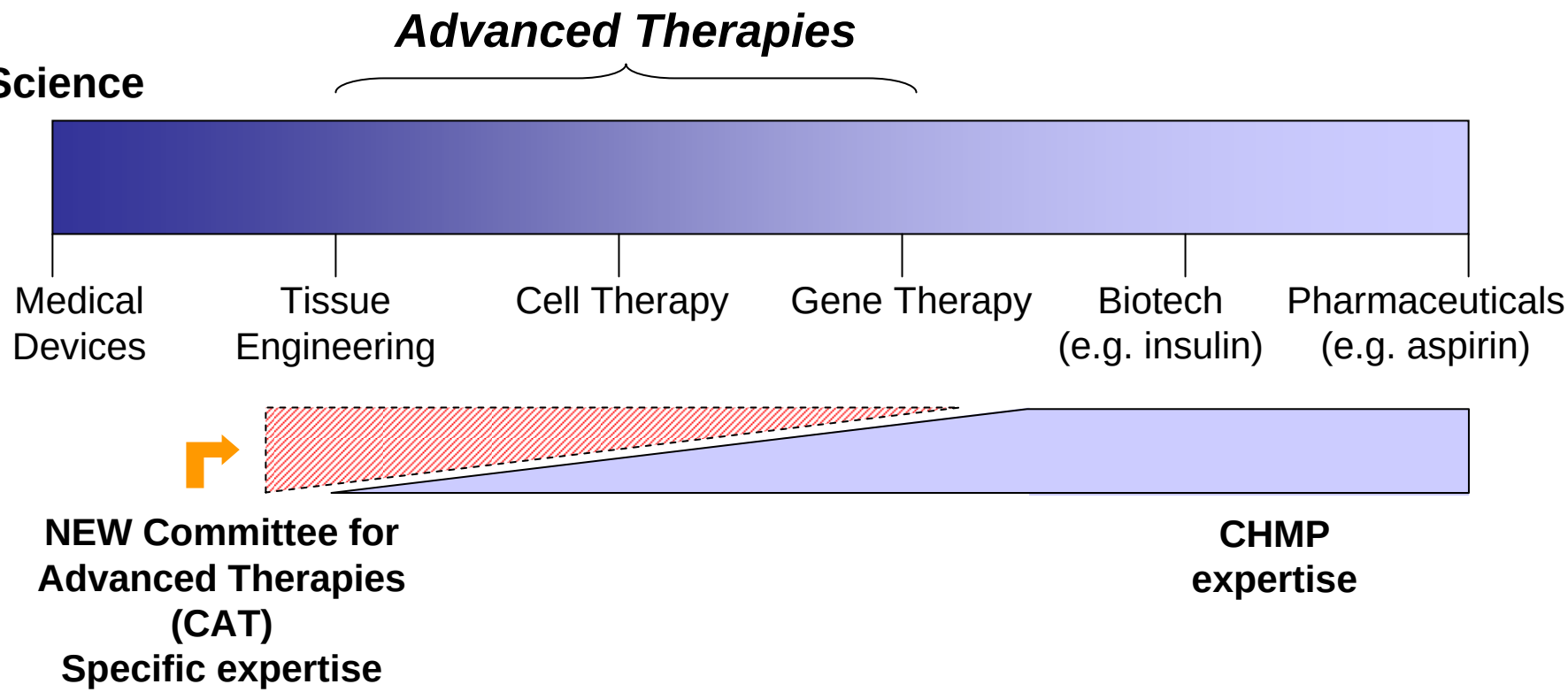
Tissue Engineered

Bridging the gap

Legislation



Science



Regulation on Advanced Therapies
Key elements

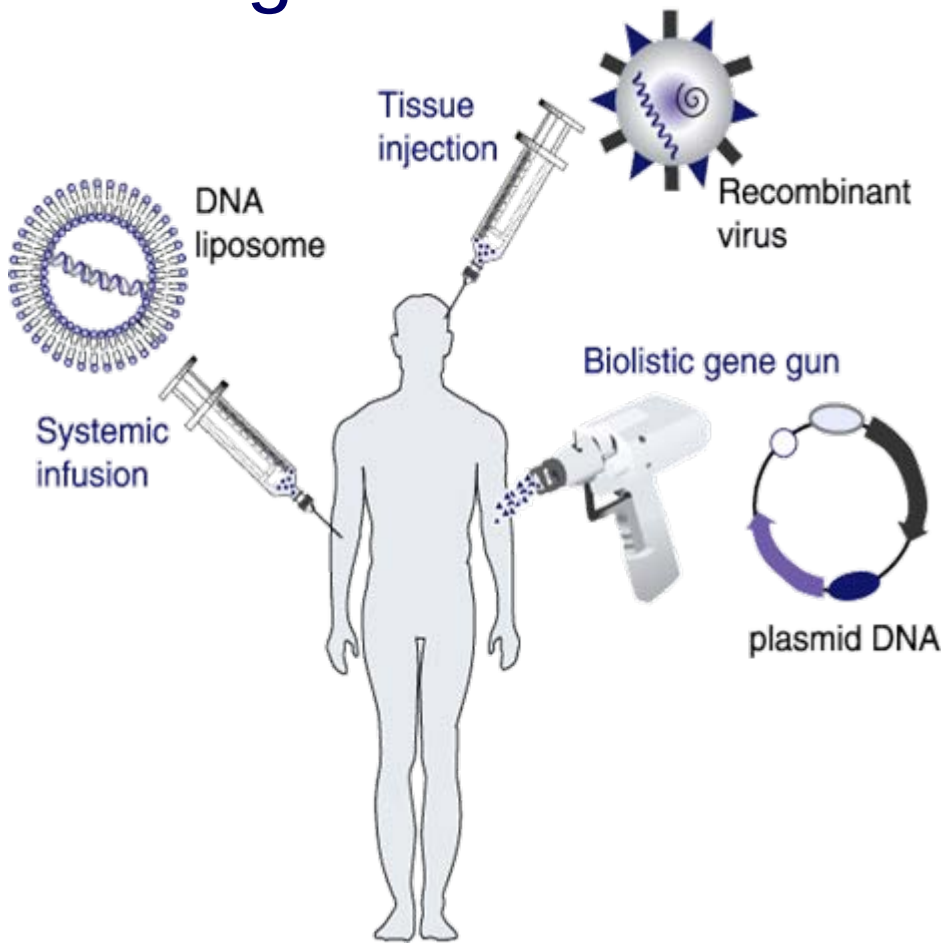
- Advanced Therapy medicinal products (ATMP)
  - Gene therapy products
  - Somatic Cell therapy products
  - Tissue engineered products

- Principles of existing legislation on medicines apply to advanced therapies:
  - Marketing authorisation
  - Quality, Safety & Efficacy
  - Post-authorisation vigilance

What is a gene therapy product?

- Medicinal product aiming at the transfer of a functional gene into humans

- **Type of gene therapy**
  - non-specific placement
  - swap/repair a gene
  - transcription regulation
- **Vectors**
  - viral/non-viral/hybrid
- **Transduction**
  - ex vivo / in vivo
  - target cells



http://www.biochem.arizona.edu/classes/bioc471/pages/Lecture25/AMG9.11a.gif

Main Indications of Gene Therapy in Clinical Trials

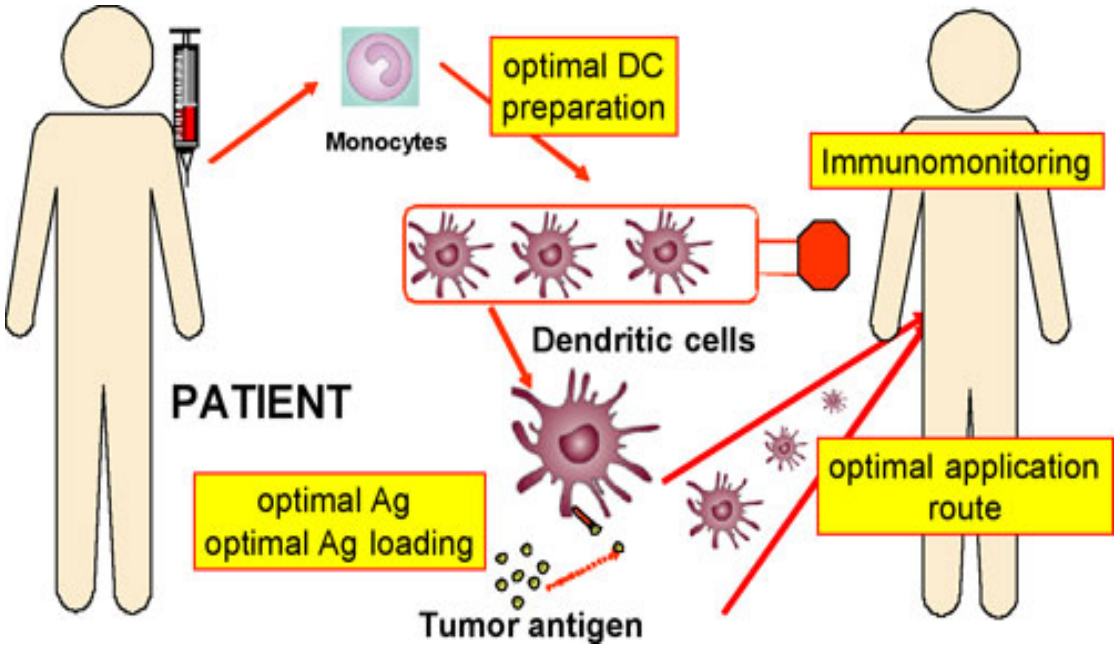
- AAT (α-1-Anti-trypsin deficiency)
- Eye diseases (AMD, inherited retinal degenerations)
- Cystic fibrosis
- Muscular dystrophies
- Severe combined immunodeficiencies
- Chronic granulomatous disease
- Coronary artery disease
- Peripheral vascular diseases
- Skin diseases (*ichtyosis, xeroderma pigmentosum, epidermolysis bullosa*)
- Lysosomal storage disorders
- Neurology (Parkinson's, Huntington's, Alzheimer's diseases)
- HIV/AIDS
- Ornithine transcarbamylase deficiency
- Blood diseases (Hemophilia, Thalasemia, Sicle cells…)
- Cancer
  - Immunotherapy
  - Oncolytic viruses
  - Suicide gene therapy

Ref: E Alton et al: Gene therapy and clinical trials. Gene Therapy (2007) 14, 1439-1447 and 1555-1563

What is a cell therapy product?

- Medicinal product based on the administration of manipulated living cells into humans
  - Cells / tissues from patient itself, from another human or from animals
  - Manipulated (engineered) cells / tissues
  - Treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues

Example: Cancer Cell therapy



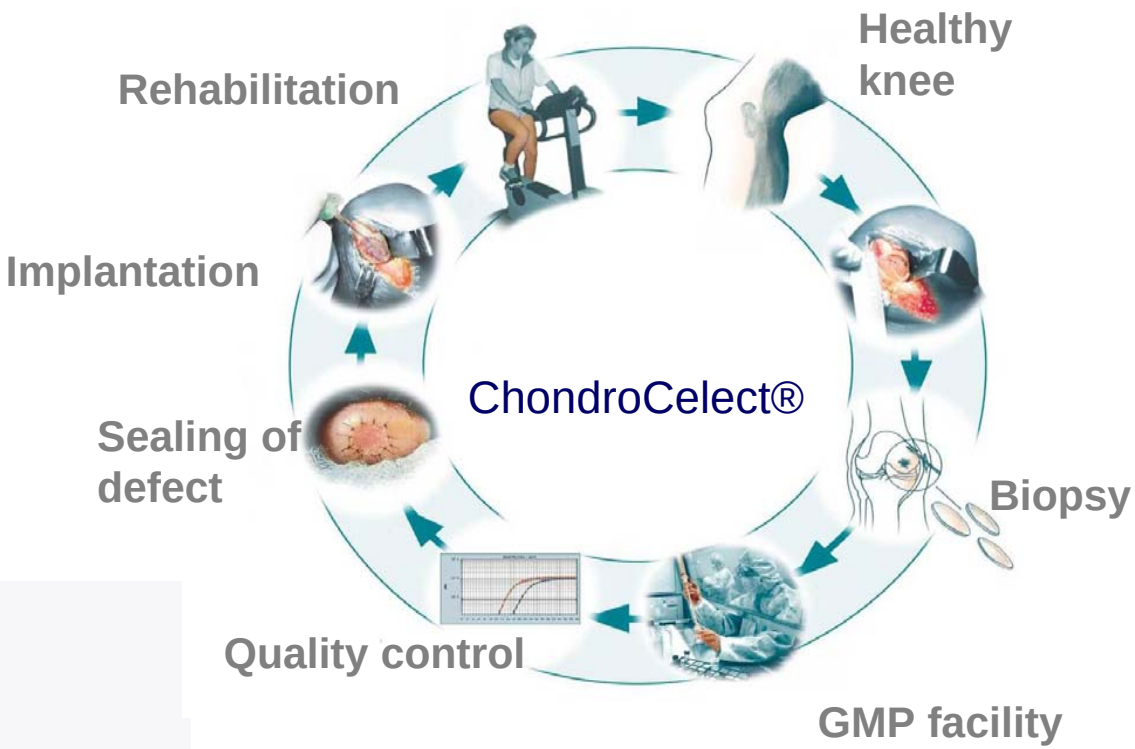
What is a Tissue Engineered product?

- Tissue Engineered products (TEP)
  - Contain/consist of engineered cells/tissues
  - Must contain viable cells
  - Administered to human to regenerate, repair or replace a human tissue

- Examples:
  - Artificial skin (burn wounds)
  - Cartilage repair
  - Neo-organs

Example: Cartilage repair

First generation →



Second generation

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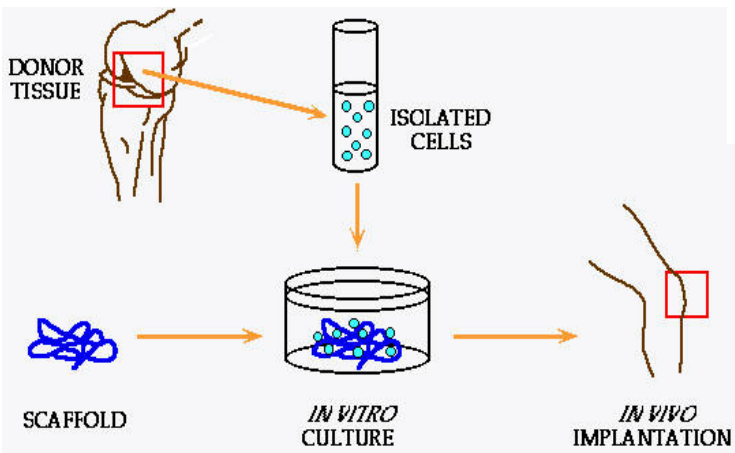


Evaluation procedure for ATMP

- Centralised procedure mandatory:
  - pooling of Community expertise
  - harmonised requirements & evaluation
  - ensure uniform and direct access to market

- Single evaluation and authorisation for the entire EU

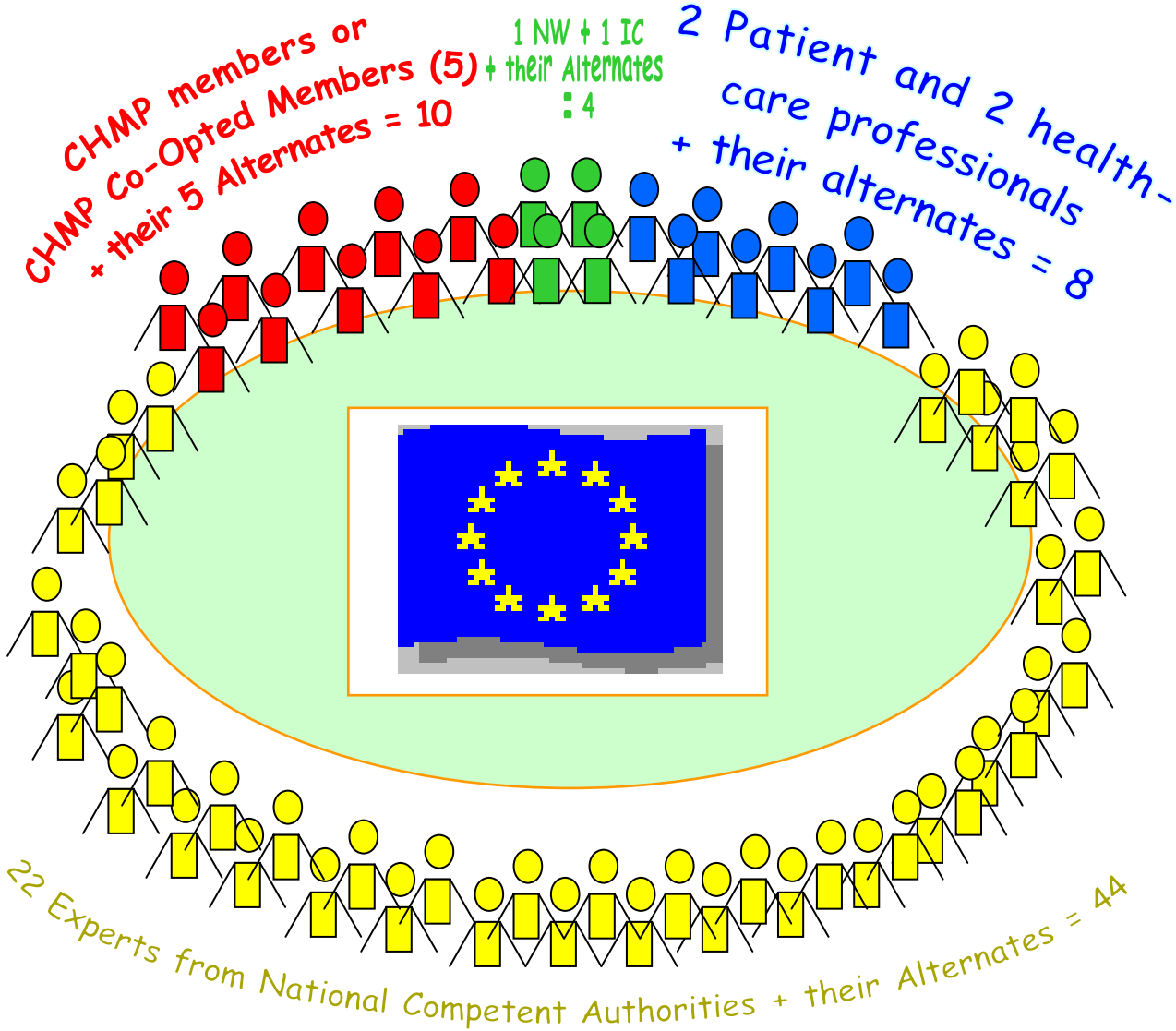
Evaluation procedure for ATMP

- New Committee for Advanced Therapies (CAT)
  - Legislation defines composition / expertise
  - Main tasks: To evaluate & prepare draft opinions on ATMP
    - For final approval by CHMP
  - Involvement in Scientific Advice on ATMP
  - Additional (new) tasks such as:
    - Certification of Quality / Non-clinical data (for SMEs)
    - Scientific recommendation on classification as ATMP
    - Evaluation of products already on the market

CAT COMPOSITION

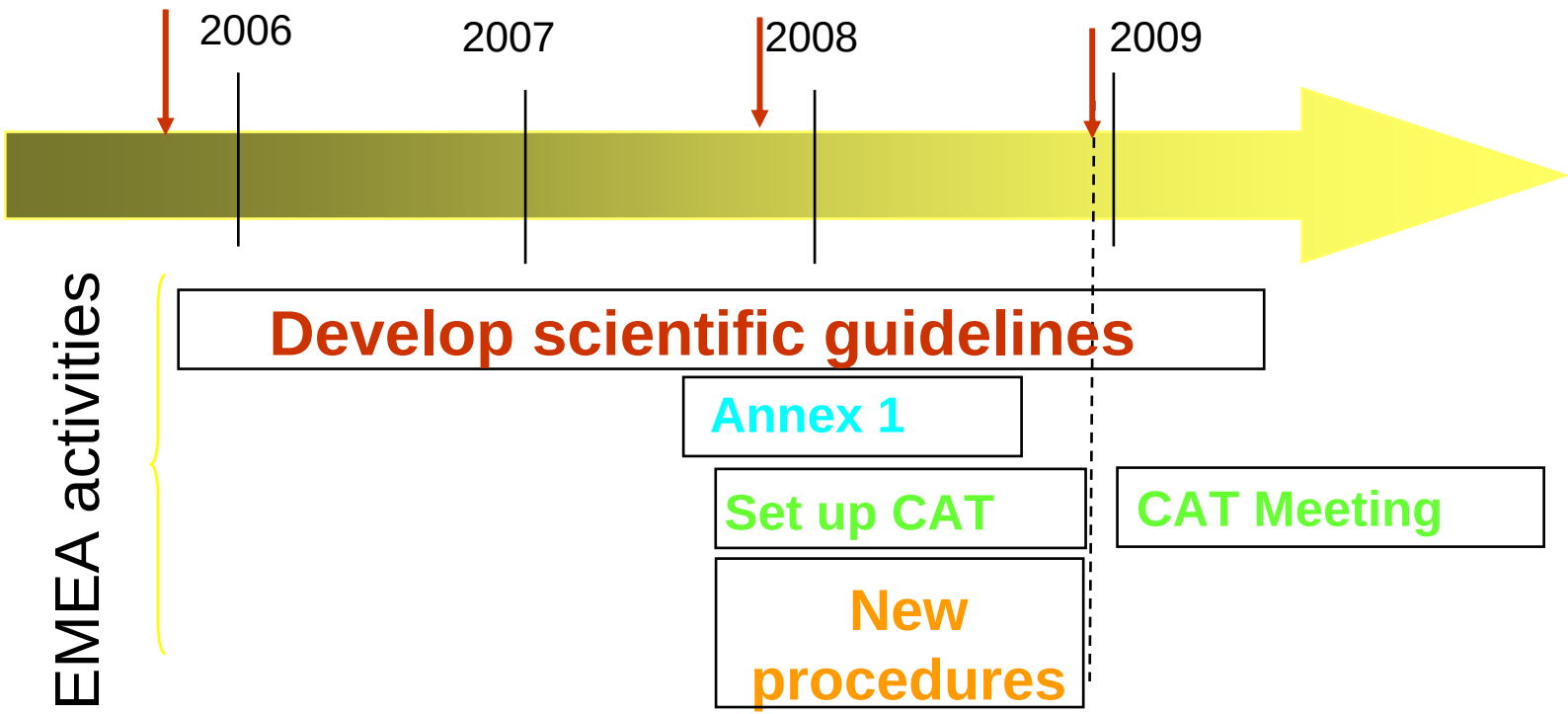
CAT should covers the scientific areas relevant to advanced therapies, including:

- **Medical devices** [2+2 at least],
- **Tissue engineering,**
- **Gene therapy,**
- **Cell therapy,**
- **Biotechnology,**
- **Surgery,**
- **Pharmacovigilance,**
- **Risk management and**
- **Ethics.**



EMEA Implementation of ATMP Regulation

Nov 2005	December 2007	End Dec. 2008
ATMP Regulation Proposal	Publication ATMP Reg. 1394/2007	Application of Reg. 1394/2007



Development of Guidelines

- A lot of Scientific guidelines already in place:
  - Overaching GL on gene transfer medicinal products
  - Overaching GL on cell-based medicinal products (somatic cell therapy + tissue engineered products)
  - Specific guidelines e.g.
    - Quality/manufacture of lentivirus vectors (GT),
    - Non-clinical testing before first use of GT product in man

- Guidelines under development, for example:
  - GL on clinical monitoring and follow-up of patients expose to GTMP
  - GL on the application of the risk analysis approach for cell-based medicinal products in pre- and post-authorisation phase

Development of technical requirements

- Scientific input by EMEA/CHMP & Working Parties in the development of 'dossier requirement'
  - For gene therapy MP (revision), somatic cell-therapy MP (revision) and Tissue engineered product (new)
  - Requirements specific for / adapted to ATMP
  - Additional flexibility where needed for new class of ATMPs

- Revision of Annex I to Dir. 2001/83

More information on Advanced Therapy Medicinal products

- EMEA

http://www.emea.europa.eu/htms/human/mes/advancedtherapies.htm

- Commission

http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/advanced_en.htm

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EMEA and Oncology Biological Products

- EMEA is responsible for the licensing of medicinal products via the centralised procedure
- Responsibility for the approval of clinical trials is with the EU Member State where the trial in conducted

Concluding remarks

- Oncology (Biological) Products will all be authorised via the centralised procedure:
  - Recombinant products
  - Biological products (e.g. cell lysates)
  - Advanced therapy products:
    - Cell therapy products: dendritic cells loaded with cancer antigens
    - Gene therapy products
  - Also: New chemical entities

Concluding remarks

- All companies developing oncology (biological) products should contact EMEA for assistance:
  - SME status
  - Orphan drug status
  - Scientific advice
  - Marketing authorisation application

How to contact EMEA

- General queries, Request for briefing meetings or Request for regulatory Classification

  http://www.emea.europa.eu/htms/human/mes/itf.htm
- SME Office

  http://www.emea.europa.eu/SME/SMEoverview.htm
- EMEA Scientific advice procedure

  http://www.emea.europa.eu/htms/human/sciadvice/Scientific.htm
- EMEA Orphan drug designation

  http://www.emea.europa.eu/htms/human/orphans/intro.htm


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