Implementation of Advanced Therapies

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Content

- "Medicinal Product" type
- Access to European Expertise
- Provision Regulatory Framework for Industry
- Centralised Review Process

Regulation on Advanced Therapies (Regulation (EC) 1394/2007)

Legislation

- ATR Reg. 1394 / 2007

Science

- Advanced Therapies
- Medical Devices
- ATC
- Science

- ATR Reg. 1394 / 2007

- Medical Device
- EU
- Regulation
- Committee
- Advanced
- Therapies
- CAT

- CHMP
- Expertise
- Specific expertise

Regulation on Advanced Therapies

Key elements

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

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

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 (Ichthyosis, xeroderma pigmentosum, epidermolysis bullosa)

- Lysosomal storage disorders
- Neurology (Parkinson’s, Huntington’s, Alzheimer’s diseases)
- HIV/AIDS
- Ornithine transcarbamylase deficiency
- Blood diseases (Hemophilia, Thalassemia, Sickle cells…)
- Cancer
  - Immunotherapy
  - Oncolytic viruses
  - Suicide gene therapy

What is a cell therapy product?
- Medicinal product based on the administration of manipulated 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
  - Administered to human to regenerate, repair or replace a human tissue

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

Tissue engineered products

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

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.

[Recait 9 & Art. 21]
Development of new procedures

- Tasks of CAT: procedures/procedural guideline
  - Evaluation of MAA for ATMP
  - Preparation of draft Opinion for adoption by CHMP within 210 days
  - Interactions with Notified Bodies (combined ATMP)
  - Re-examination procedure
  - Scientific classification of ATMP
  - Scientific advice (contribution to SAWP)

Regulation on Advanced Therapies

Key elements

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

Development Life Cycle ATPs

GMP and GCP for ATMP

- Guidelines to reflect specificities of ATMP: discussions ongoing

- But: No change to Dir 2003/94/EC (GMP) / 2001/20/EC (GCP) / Dir 2001/83/EC (Title IV – Manufacture and importation)

Gene Therapy Products

Development of Guidelines

- Multidisciplinary GL on gene transfer MP
- Lentiviral vector, quality & manufacture
- Inadvertent Germline transmission
- medicinal products containing genetically modified cells
- non-clinical studies required before first clinical use of gene therapy medicinal products
- on clinical monitoring and follow-up of patients exposed to gene therapy/gene transfer medicinal products
- Environmental risk assessment of gene therapy medicinal products

Cell-based Medicinal Products

Development of Guidelines

Guideline on cell-based medicinal product

- Xenogenic cell therapy products
- Tissue engineered products
  - Multidisciplinary GL (Quality, Non-clinical, Clinical)

- Revision of the PtC on Xenogenic cell therapy medicinal product
- GL on clinical follow-up of patients exposed to cell-based medicinal products
- Multidisciplinary GL on Xenogenic Cell Therapy MP
Dossier requirements

- GTMP (revision), somatic CTMP (revision) and TEP (new)
  - Will become part of Annex I of Directive 2001/83/EC
  - Draft published by the EC for external consultation
- Annex I will address:
  - Requirements specific for ATMP
    - E.g. Interactions between cells and structural components
  - Additional flexibility where needed for ATMP

Traceability

Input in GL development by EC

- 3 levels of traceability to work together:
  - From donor to tissue establishment /DG Sanco
  - From receipt of cells/tissue in pharmaceutical facility to the delivery of cell-based product at the hospital
  - From receipt in hospital to administration to patients & patient follow-up if required
- MAH responsible for the system for traceability
- Sourcing to delivery

CAT-CHMP interactions

Assessment Team 1

CHMP Rapporteur
CAT Rapporteur
Q / S / E (ATP) experts

Assessment Team 2

CHMP Co-Rapporteur
CAT Co-Rapporteur
Q / S / E (ATP) experts

Implementation of the Advanced Therapies Regulation

Nov 2005 ATMP Regulation Proposal

EMEA activities

- Setting up CAT
- Annex I
- Development of scient. guidelines
- New procedures
Products legally on market