Introduction to Advanced Therapy Medicinal Products Regulation

-Regulation (EC) No.1394/2007

-Regulation (EC) No. 668/2009

-Directive 2009/120/EC

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Presentation Outline

1. Outline of the legislation-Regulation.

2. Evaluation of Advanced Therapies at the EMEA-Procedures.

3. Incentives in legislation.

4. Summary/Take home messages.

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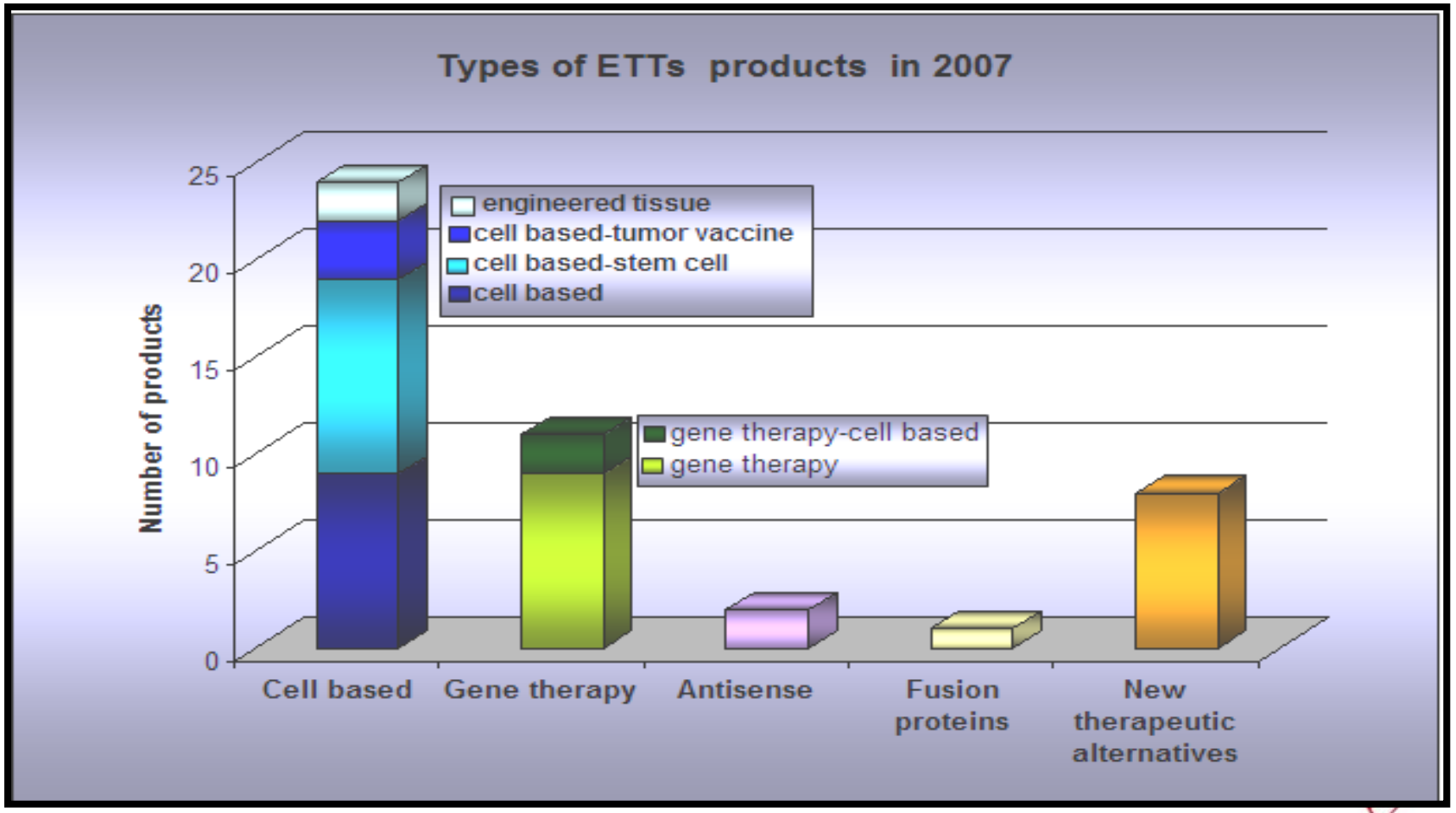
Overview of Emerging Therapies and Technologies experience at the EMEA*



Courtesy of EMEA

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Advanced Therapies: the need for Regulation

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Tags # HEALTH # SCAM # STEM CELL # STEM CELL RESEARCH

Irish patients scammed by bogus stem cell therapies abroad

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SERIOUSLY ILL IRISH patients have been travelling abroad in search of stem cell therapies after falsely being assured that their conditions will be improved or cured.

People hoping to find relief from serious conditions such as multiple sclerosis (MS) and spinal injuries, amongst others, have been attracted to clinics abroad that offer risky treatments which Irish medical

Pictured: a frozen vial of human embryonic stem cells

Image: Paul Sancya/AP/Press Association Images

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Stem cell firm uses Swansea ferry to evade Irish block on controversial treatment

- Hundreds of UK patients book £12,000 injections
- Irish Medicines Board acts to stop treatment in Cork

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Sarah Boseley, health editor
The Guardian, Monday 1 May 2006 01.17 BST

Article history

A company offering controversial "stem cell" injections to hundreds of people from the UK with multiple sclerosis and other neurological diseases is planning to get around a ban on treatment in Ireland by carrying it out in international waters on an overnight ferry.

Advanced Cell Therapeutics (ACT), which has an address in Geneva and a London telephone number, has been supplying stem cells from umbilical cord blood to 12 clinics around the world, of which two are in the Netherlands and one in Spain. Demand from the UK - where the treatment is illegal - has been huge, following tabloid newspaper stories

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Advanced Therapies: the needs

- Specialised expertise to guarantee the best scientific evaluation of benefit/risk balance
- Legal certainty and suitable rules in a predictable, reliable, accountable and integrated EU system
- Transparency, collaboration, communication

for the benefit of patients

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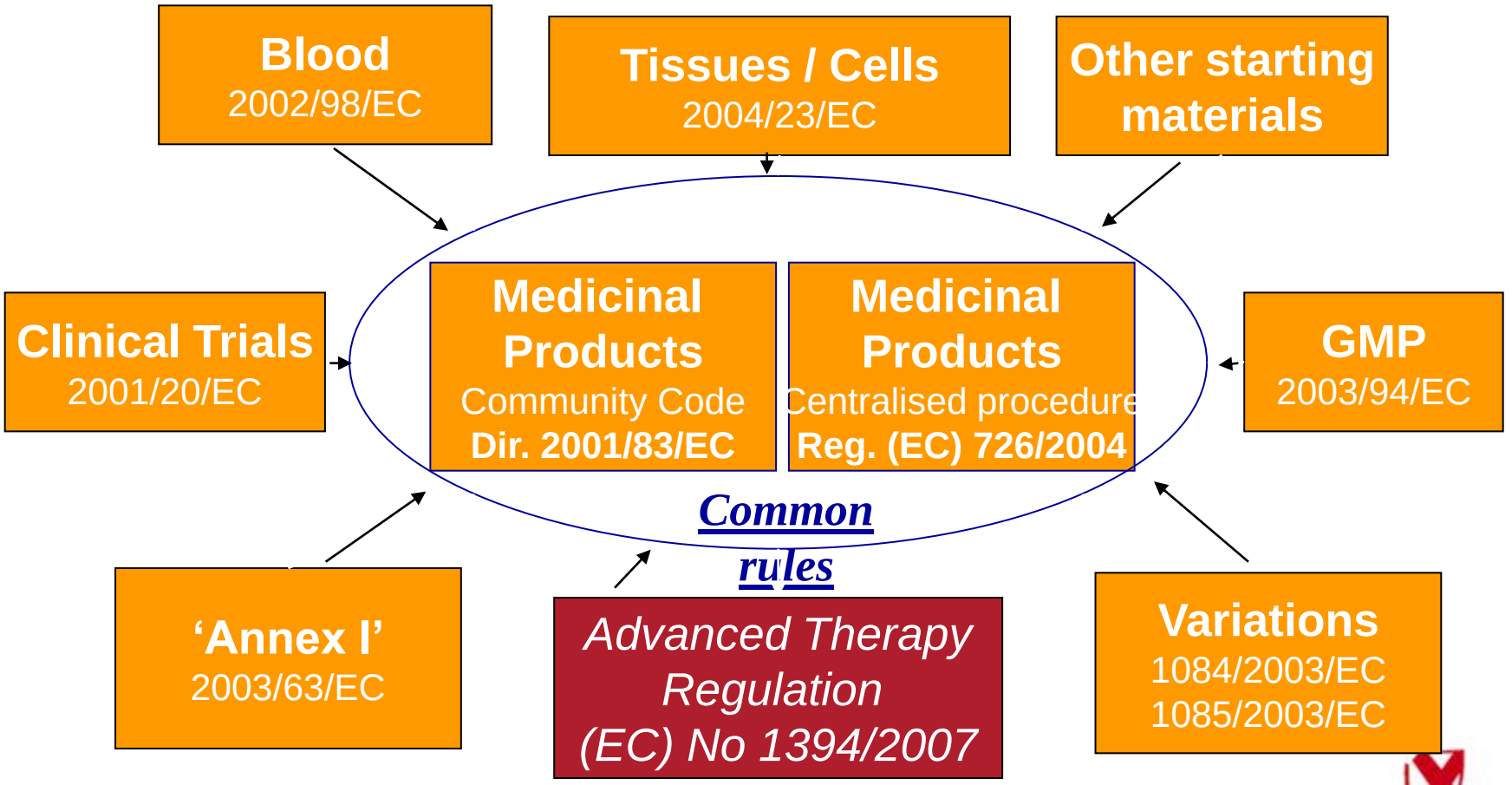
EU Legal/regulatory framework for medicinal products



*"This Regulation lays down **specific** rules concerning the authorisation, supervision and pharmacovigilance of advanced therapy medicinal products."*

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Key principles of the ATMP Regulation

For products within the scope:

- No marketing without prior authorisation
- Demonstration of Quality, Safety & Efficacy
- Post-authorisation vigilance
- Centralised procedure mandatory

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Summary of Chapters/Articles Regulation 1394/2007

Came into effect 30 December 2008

Chapter 1-**Definitions and Scope**
Chapter 2-**Marketing Authorisation Requirements**
Chapter 3-**Evaluation Procedures**
Chapter 4-**Summary of Product characteristics and labelling**
Chapter 5-**Post-Authorisation Requirements**
Chapter 6-**Incentives**
Chapter 7-**Committee for Advanced Therapies**
Chapter 8-**General Provisions**

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

- Regulation 668/2009-Evaluation and **Certification** of Non-clinical & Quality data of ATMPs by micro-small and medium sized SMEs

- Directive 2009/120/EC-amending Directive 2001/83/EC replaces part IV of Annex 1

(Module 3,4,& 5**:Risk Based Approach** Guideline)

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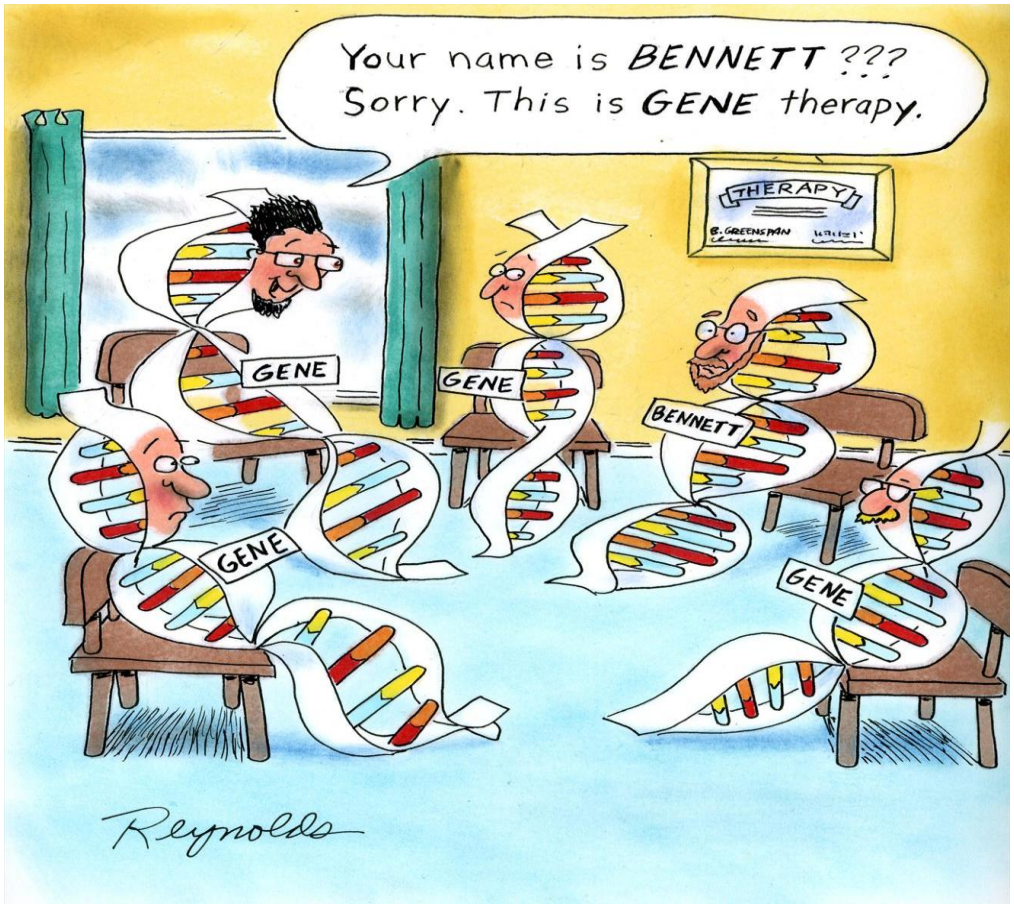

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Gene Therapy Medicinal product means a biological medicinal product which has the following characteristics

(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, 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.

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

Somatic Cell Therapy Medicinal Product means a biological product which has the following characteristics

(a) Contains or **consists of cells or tissues** that may have been subject to **substantial manipulation(annex** 1) so that biological, 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.

(b) Is presented as having properties for, 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 it's cells or tissues.

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Non-Substantial manipulation
Annex 1

- cutting,
- grinding,
- shaping,
- centrifugation,
- soaking in antibiotic or antimicrobial solutions,
- sterilization,
- irradiation,
- cell separation,
- concentration or purification,
- filtering,
- lyophilization,
- freezing,
- cryopreservation,
- vitrification.

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

Tissue Engineered Product

(a) contains or consists of **engineered cells** or tissues

(b) 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.**

Cells or tissues shall be considered engineered

1. if they have been subjected to **substantial manipulation** so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved.
2. Cells or tissues are **not intended** to be used for the **same essential function** or functions in the recipient as donor.

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Evaluation procedures

- Marketing Authorisation
- Classification
- Certification
- Scientific Advice

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- Marketing Authorisation Applications

Same principles as normal Centralised procedure:

-Scientific opinion by Day 210 to Commission
– Evaluation by two independent teams
– Rapp/CoRapp are from CAT, not CHMP
– CAT adopts LoQ, LoOI and draft opinion
– CHMP will still adopt the final opinion at D 210

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

- Reduction of fee for marketing authorisation-50% if Applicant is hospital or SME and can prove public health interest. Also applied to post marketing activities for first year. Applies to transitional period. Products legally on market MAA free until 2011-2012.

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- Classification

– Open to all applicants

– Scientific Recommendation from CAT on the Regulatory Classification of their ATMP

- 60-day procedure

– Publication of summary information

- Free procedure

- Orphan drugs-designation free, SA free, reduction in MAA fee.

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- Certification Procedure

Only for SMEs

- Scientific evaluation by CAT of
  - (early) quality / development data (Module 3)
  - (early) non-clinical data (Module 4)
- Evaluation to the scientific standards of a MAA

- If positive evaluation: Certification by EMA

- The SME applicant will receive the evaluation report (and List of issue)

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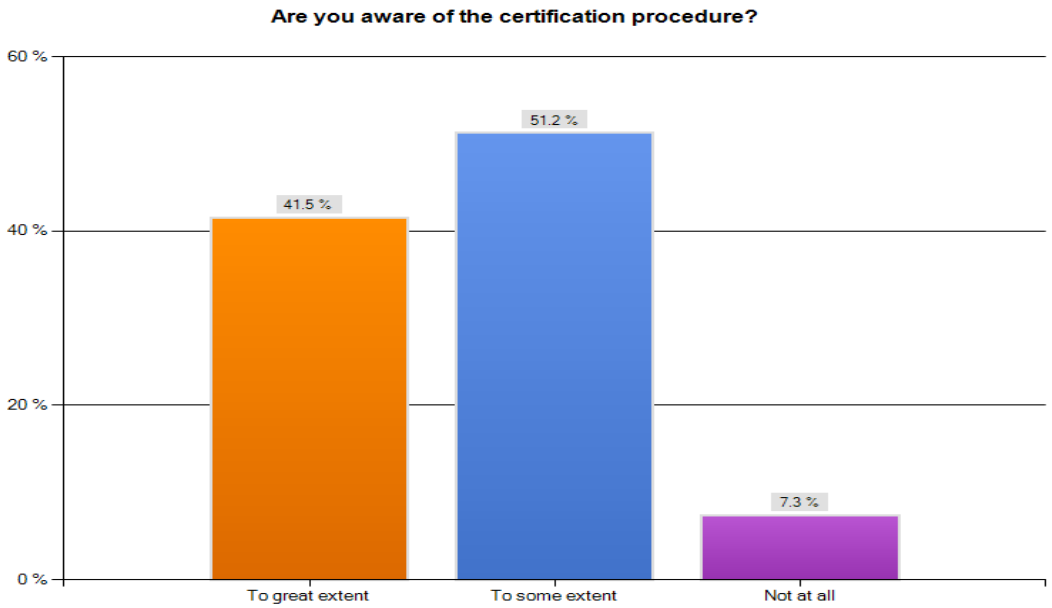
- Certification Procedure-EMA survey

Why Procedure not more widely utilised?



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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

- The certification procedure is perceived to be a valuable incentive from SMEs developing ATMPs.

- Suggested to possibly extend the scope of the certification procedure.

Concerns-

- The absence of a link between certification and marketing authorisation.

- The overlap with formal scientific advice.

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

- Scientific Advice

75 Day procedure

Quality
Preclinical
Clinical

Fees payable for scientific advice in respect of ATMPs,
90% reduction for SMEs
65% reduction for other Applicants

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Incentives

- Regulatory Procedures
- Financial incentives
- Dedicated Expertise
- Support to Applicants

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

Dedicated Expertise

- Dedicated EMA Secretariat, Procedural advices, links to other EMA sections(paediatrics, SME office)
- Scientific Advice, Presubmission meetings- recommended for ATMPs, return for clarifications and follow up advice as often as needed.
- Committee for Advanced Therapies
- Scientific Guidelines

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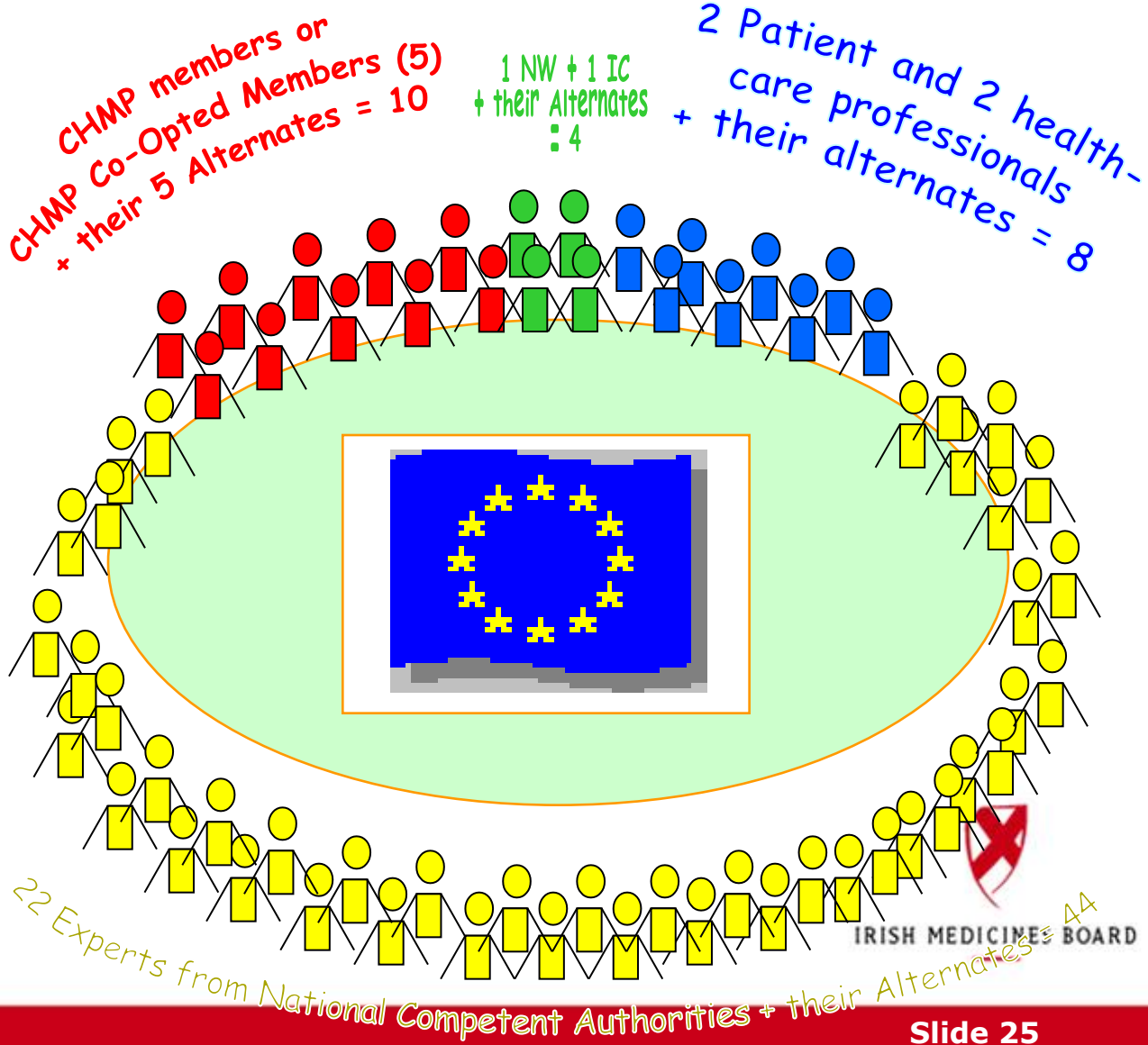
CAT COMPOSITION

CAT should cover 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.**



Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

Support to Applicants

- Innovation Task Force briefing meetings
- SME office
- IMB-Role

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

Innovation Task Force

- Briefing meetings

– Aimed at early contacts with companies developing innovative medicines & ATMPs

– Information on next steps

- ATMP classification / certification
- Involvement of CAT or WP members
- Not binding / high level input
- Not to replace the Scientific Advice procedure

ITFsecretariat@ema.europa.eu

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Regulation 1394/2007,Regulation 668/2009,Directive 2009/120/EC

- SME office

-to facilitate and promote interaction, partnering and networking between SMEs;

-to increase information available to SMEs and their stakeholders;

-to provide a source of information for European Union (EU) institutions, agencies and Member States.

smeoffice@ema.europa.eu

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Article 28-Scope of ATMP Regulation

- Exclusion under very specific conditions (‘**Hospital exemption’ article**):

  - Non-routine basis of production
  - Specific quality standards
  - Used in same MS (manufacturing authorised by Comp. Authority of MS)
  - Custom-made product for individual patient
  - Under the exclusive professional responsability of a practitioner
  - IMB Guidance

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Article 29-Transitional Period

- Refers to products legally on market

Advanced therapy medicinal products, other than tissue engineered products, which were legally on the Community market in accordance with national or Community legislation on 30 December 2008, shall comply with this Regulation no later than 30 December 2011.

Tissue engineered products which were legally on the Community market in accordance with national or Community legislation on 30 December 2008 shall comply with this Regulation no later than 30 December 2012.

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Article 4-Clinical Trials

Regulation 1394/2007

- Clinical trials on ATMPs should be conducted in accordance with overarching principles and ethical guidelines of 2001/21/EC & 2005/28/EC.
- Extended timelines apply to clinical trials with ATMPs.
- New Clinical Trial legislation.
- CTFG-VHP(voluntary harmonisation procedure).

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Article 14 &15

- Long Term Follow-up

Efficacy & Safety

Guideline on Safety and Efficacy follow-up-Risk Management of Advanced Therapy Medicinal Products

- Traceability

Patient and Product traceability

30 years MAH

2004/23/EC

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Guidelines

London, 08 April 2010
EMA/CAT/CPWP/568181/2009
Committee For Advanced Therapies (CAT)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Reflection paper on *in-vitro* cultured chondrocyte containing products for cartilage repair of the knee

Final

Adoption by CAT	16 April 2010

- **Procedural**

-Certification, Classification, Post-Authorisation requirements

- **Scientific**

-Risk Based Approach guideline

-Genetherapy

-Cell Therapy &Tissue engineered Products

-Biological-BWP

EMA website-Regulatory > Human medicines > Advanced therapies.

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Take Home Messages

- Regulation 1394/2007 –
  Defines ATMPs and outlines the procedures for Evaluation of Advanced Therapies.

- Incentives for development of ATMPs include classification of Advanced therapies, certification of quality and non-clinical data, scientific advice, reduced fees for MAH applications, access to available expertise and support-ITF, SME office EMA

- Scientific and Regulatory guidelines for Gene, Cell and Tissue engineered products are in place

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Thankyou; Any Questions?

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