

cell/tissue engineered products

- French experience
- European experience

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Disclaimer

- ✓ *I attend this conference as an individual expert and, although being a member of the CAT and BWP, my presentation might not be the view of the EMA and any of their Committees or working parties and neither of the French Medicines Agency (Afssaps).*
- ✓ *The views expressed here are my personal views, and may not be understood or quoted as being made on behalf of the EMA or Afssaps and binds in no way the organisations mentioned before.*

Presentation outlook

- ✓ The two regulatory status in Europe for « cell/tissue [engineered] products »
 - Tissues and cells directive
 - Advanced therapy medicinal products
- ✓ French experience and organisation
- ✓ European approach for ATMP
- ✓ CAT activities
 - Dossier evaluation
 - Classification
 - Scientific advice
 - Technical guidelines
 - Certification
- ✓ Conclusion

« cell/tissues [engineered] products »

What are we speaking about?

- ✓ In Europe, two distinct regulatory systems:
 - Human tissue and cells → Directive 2004/23
 - Advanced Therapy Medicinal products → Regulation 1394/2007

Human tissues and cells Directive -1-

DIRECTIVE 2004/23/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 31 March 2004

on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

✓ And subsequent directives

- [DIRECTIVE 2006/17/EC](#) on technical requirements for the donation, procurement and testing of human tissues and cells
- [DIRECTIVE 2006/86/EC](#) on traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells

- ## ✓ This Directive shall apply to the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells intended for human applications and of manufactured products derived from human tissues and cells intended for human applications.

Human tissues and cells Directive - 2-

The main chapters of Tissues and cells directive:

✓ Article 3 : Definitions

- Tissue establishment: means a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells;

Human tissues and cells Directive - 3-

The main chapters of Tissues and cells directive:

- ✓ Article 4 : National competent authorities responsible for implementing the requirements
 - ✓ Article 5 : Supervision of human tissue and cell procurement
 - ✓ Article 6 : Accreditation, designation, authorisation or licensing of
 - tissue establishments
 - tissue and cell preparation processes
 - ✓ Article 7 : Inspections and control measures
 - ✓ Article 8 : Traceability: from the donor to the recipient and vice versa.
 - ✓ Article 9: Import/export of human tissues and cells
 - ✓ Article 10: Register of tissue establishments and reporting obligations:
 - record of activities by tissues establishments
 - competent authorities to maintain a publicly accessible register of tissue establishments
 - ✓ Article 11: Notification of serious adverse events and reactions:
 - Member States shall ensure that there is a system in place to report, investigate, register and transmit information about serious adverse events and reactions
- ➔ It is the Member States responsibilities to put in place the necessary regulatory framework to authorise, follow-up and monitor activities in the field of “tissues and cells” Which are not considered as “medicinal products” .

Human tissues and cells Directive - 4-

- ✓ The « Human tissues and cells » directive
 - Covers tissues and cells obtained from donation (autologous or allogeneic), intended for human application
 - Introduce the notion of
 - donation and procurement
 - testing and processing
 - preservation, storage
 - distribution of human tissues and cells
 - Introduce the definition and concept of
 - « tissue Establishment » authorised by National Competent Authorities,
 - National competent authorities responsible for accreditation, inspection, of the establishment(s) on their territory and vigilance → National duties for implementation of the Directive
- ✓ Human tissues and cells are not considered as medicinal products (and thus not all pharmaceutical requirements are applicable)
- ✓ However, « manufactured products » can be derived from those tissues and cells collected in « tissue establishments » and will be regulated by other regulation
- ✓ Human Tissues and Cells are under the responsibilities of tissue establishments and the “market” is relatively limited to national territory and use.... More for hospital use and for “conventional application”.
- ✓ This contrast with the other types of “medicinal products” which may be derived from Human Tissues and Cells, designated as “advanced therapy medicinal products” (ATMPs) and covered now by the pharmaceutical legislation

Advanced Therapy Medicinal Products (ATMP)

- ✓ Second regulatory status possible in Europe for « cell/tissue [engineered] products »
- ✓ Regulation 1394/2007

EN

Official Journal of the European Union

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

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF>

Regulation 1394/2007

Article 1

Subject matter

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

Article 2

Definitions

1. In addition to the definitions laid down in Article 1 of Directive 2001/83/EC and in Article 3, points (a) to (l) and (o) to (q) of Directive 2004/23/EC, the following definitions shall apply for the purposes of this Regulation:

(a) 'Advanced therapy medicinal product' means any of the following medicinal products for human use:

— a gene therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,

— a somatic cell therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,

— a tissue engineered product as defined in point (b).

✓ Classifying tissue-based or cell-based products as medicinal products → pharmaceutical legislation applies in all aspects of the product life cycle:

- Development and Clinical trials
- GMP for the production/quality control
- Pharmacovigilance
- With additional requirements (long term follow up –art.14)

✓ EMA responsible for the regulatory framework

✓ One centralised Marketing Authorisation

✓ One scientific Committee to deal with the submission : CAT

European Regulatory Framework for tissues and cells products

Medicinal Products

Tissues/Cells

Community Code
Directive 2001/83/EC
(Annex 2003/63/EC)

**Regulation
Advanced Therapy
Medicinal Products
1394/2007/EC**

Directive 2004/23/CE
Donnor selection (2006/17)
Establishment., GP, traceability (2006/...

**New Chemical
Entity
MP**

**Biological
MP**

**Gen
e Th** | **Cell
Th**

*Med Products
Annex 1*

**Tissue
Engineered
Products**

cell/tissue not ATMP

MA
Centralized or National

MA
Centralized mandatory

**National autorisation
system**

**Pharmacovigilance
Clinical Trials (Directive 2001/20)**

**Biovigilance
and clinical trials (France)**

The two regulatory status

	Dir. 2004/23 → National responsibilities	Reg. 1394/2007 → European framework
Product	Not considered as « medicinal product » but - Cell preparations - Tissues	Medicinal products: ATMP
Authorisation	National Authorisation(s)	EU centralised Marketing Authorisation
Establishment	« Tissue establishment » National accreditation (for France Tissues or cells establishment)	Pharmaceutical establishment Authorisation by National competent Authorities
Manufacturing practice	Based on the principles of cGMP with adaptation for Tissues and Cells (Dir. 2006/86) At the discretion of National authorities	GMP mandatory ATMP production covered in annex 2 of the EU cGMP (public consultation on going)
Dossier	National decision (in France adaptation of the CTD)	CTD format
Vigilance	National decision (in France « Biovigilance » is mandatory)	Pharmacovigilance + long term follow up
Clinical trials and GCPs	National decision (in France case by case, well established use or clinical trial evidence)	Mandatory to establish the risk-benefit profile and claimed indication(s)

Importance of classifying those products

- ✓ Importance of the definition /classification chosen, examples given:
 - T2c001™: Autologous bone marrow-derived mononuclear cells
 - a bone marrow aspirate followed by a ficoll centrifugation,
 - Acute myocardial infarction: cardiac re-injection in the left ventricle
 - → considered as ATMP, cell therapy
 - Chondroselect™:
 - autologous chondrocytes, expanded from a cartilage biopsy
 - reimplanted in the cartilage defect
 - → ATMP, cell therapy
 - freeze-dried thrombocytes,
 - for application is any wound healing (orthopedics, dental surgery)
 - → not considered as medicinal product, to be regulated by Dir. 2004/23
- ✓ The « process » and final product and its claim(s) → qualify or not as « medicinal products »
- ✓ The autologous origin of the cells is not the only criteria to justify not being classified as medicinal product and not being imposed clinical trials and clinical evidence

Presentation outlook

- ✓ The two regulatory status in Europe for « cell/tissue [engineered] products »
 - Tissues and cells directive
 - Advanced therapy medicinal products
- ✓ **French experience and organisation**
- ✓ European approach for ATMP
- ✓ CAT activities
 - Dossier evaluation
 - Classification
 - Scientific advice
 - Technical guidelines
 - Certification
- ✓ **Conclusion**

French organisation for « tissues and cells »

- ✓ In France, Afssaps is the Competent Authorities for regulating the two status
- ✓ The same department in Afssaps is in charge of dealing with the two types of products

Afssaps mandates and responsibilities

- ✓ Afssaps is in charge of authorising or accrediting
 - Tissues or cells Establishments
 - Private or Public organisations
 - Pharmaceutical establishment for ATMP
- ✓ Products to be authorised by Afssaps
 - Tissues or cells preparations (according to Dir. 2004/23): authorisation for a “preparation” (cells) or a “process” (tissues)
 - ATMP under the “hospital exemption” status
- ✓ Clinical trials
 - During the development of ATMPs
 - For qualification of the “tissue” or “cell preparation” to be authorised for use in France
- ✓ Other Responsibilities:
 - Inspection
 - Manufacturing sites for medicinal products (including ATMPs)
 - Tissue establishments
 - Academic/hospital labs involved in preparation of tissues or cell preparations used in clinical trials
 - Vigilance
 - Pharmacovigilance for medicinal products
 - Biovigilance for tissues and cells
- ✓ Quality controls of the products on the market

Cell “Preparation” Authorizations

- ✓ Cell establishments : 36
 - 50% public establishments (EFS) – 50% hospital
- ✓ Dossiers : around 140 applications for hematopoietic stem cells
 - Peripheral blood (majority)
 - Autologous
 - Allogeneic
 - Bone marrow
 - Autologous
 - Allogeneic
 - Umbilical cord blood (30 % but increasing number)
 - Allogeneic
 - CD 34+ (allogeneic peripheral HSC) only few
- ✓ Scientific data required for Quality, Safety, Efficacy (mainly well established use)

Tissue “Process” Authorizations

- ✓ Tissue establishments : 41
 - 50% held by the state establishment (EFS)
 - 40% hospital
 - 10% Private
- ✓ Dossiers : around 210 dossiers
 - Bones cryopreserved or viro inactivated
 - massive bone
 - femoral head
 - Others : iliac crest, skull bone flap...
 - Corneas
 - Keratoplasty
 - Cornea stopper
 - Skin
 - Amniotic membranes
 - Arteries, veins, valves
- ✓ Scientific data required for Quality, Safety, Efficacy (mainly well established use)

Clinical Trials in France

Cell Therapy

- ✓ Haematopoietic stem cells :marrow, peripheral, placental
 - Hematology : lymphoma, leukemia (ALL, AML...)
 - Cardiomyoplasty, lower limb arteriopathy
- ✓ Immune cells : Macrophages, dendritic, dexosomes, T cells
 - Immunotherapy of cancers (melanoma, lung, kidney, ovarian...) and infectious diseases
- ✓ Chondrocytes
 - Knee articular cartilage injuries
- ✓ Keratinocytes/ Fibroblasts
 - Venous ulcer, diabetic forefoot ulcer, second and third degree burns
- ✓ Nervous cells
 - Parkinson, huntington diseases
- ✓ Myoblasts
 - Severe postinfarction left ventricular dysfunction
- ✓ Pancreatic islets
 - Diabetes mellitus

Clinical Trials in France

Tissues

- ✓ Amniotic membrane in corneal ulcer
- ✓ Trachea replacing aorta
- ✓ Ovarian tissue auto-transplant (chemotherapy situation)
- ✓ Face transplantation
- ✓ Forearm transplantation

French activities for ATMPs

- ✓ Essentially during the development stage of those « candidate » medicinal products
 - Authorisation for Clinical trials
 - Assistance for innovation development and Scientific advice
- ✓ Contribution to EMA and CAT activities for centralised authorisations
- ✓ Other contributions
 - joint discussion with official labs, inspectors,
 - « hospital exemption » autorisation → National competences

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Consequence of the regulation -1-

- ✓ For products fulfilling the definitions (Gene therapy, cell therapy, tissue engineered):
 - Marketing authorisation before launching
 - Assessment of the Quality, Safety & Efficacy
 - Post-authorisation vigilance; specific obligation for safety and for efficacy
- ✓ Authorisation via the centralised procedure
- ✓ Same dossier as for a medicinal product (CTD) with technical adaptations)

Consequence of the regulation -2-

✓ Technical requirements:

- Pre-authorisation:
 - Compliance with 'Essential Requirements' for combined products incorporating medical devices
 - Specific guidelines on
 - GMP (Good Manufacturing Practice)
 - GCP (Good Clinical Practice)
 - Specific rules for labelling/packaging
- Post-authorisation requirements
 - Follow-up of efficacy and adverse reactions, and risk management: long term follow up → art. 14
 - Traceability

Regulation 1394/2007: the “hospital exemption” – Art. 28

- ✓ Excluded from the scope of the regulation
 - ATMP prepared in a non-routine basis (Art. 28(2))
 - Used within the same member state, in a hospital, for an individual patient
 - In that case : manufacturing is authorized by the MS. Traceability, pharmacovigilance requirements, specific quality standards at national level should be equivalent to the regulation
- ✓ “Hospital exempted products”
 - are still considered as medicinal products
 - Still considered as ATMP
 - Should be authorised by the National Competent authority
 - Following the same standards and criteria as for a marketing authorisation: *“Member States shall ensure that national traceability and pharmacovigilance requirements as well as the specific quality standards are equivalent to those provided for at Community level in respect of advanced therapy medicinal products”* (art. 28, Regulation)

Committee for Advanced Therapies (CAT)

✓ New Committee within the EMEA

- pooling of Community expertise
- multidisciplinary nature:
 - biotechnology
 - medical devices
 - risk management
 - ethics
 - ...
- representation of Civil Society and Research Community

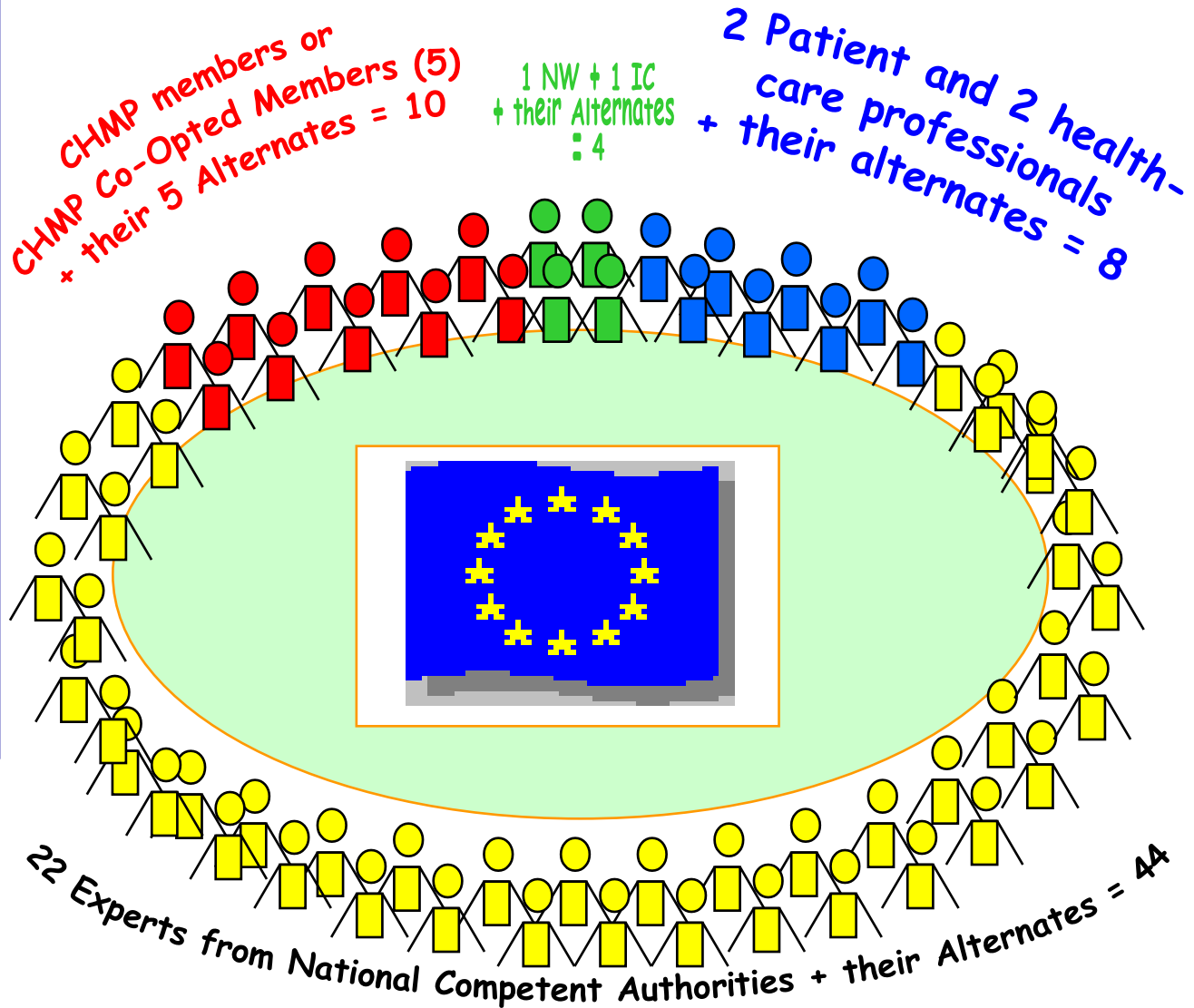
CAT COMPOSITION

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

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

[2+2 at least],

[Recital 9 & Art.21 of ATM Reg]



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Tasks of the Committee for Advanced Therapies (art. 23)

- ✓ to formulate a draft opinion on the quality, safety and efficacy of an advanced therapy medicinal product for final approval by the CHMP
→ dossier evaluation
- ✓ to provide advice, on whether a product falls within the definition of an advanced therapy medicinal product → classification
- ✓ to advise on any medicinal product which may require, for the evaluation of its quality, safety or efficacy, expertise in one of the scientific areas
→ Scientific advice
- ✓ to assist scientifically in the elaboration of any documents related to the fulfilment of the objectives of this Regulation → criteria and guidelines

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Assessment and draft opinion for authorisation

• **single application (dossier)**

• **formal acceptance by EMEA**

• **(co)-rapporteurs nominated by CAT**
• **CHMP co-ordinator + Peer reviewer**

• **rapp. assessment
by appointed experts**

• **co-rapp. assessment
by appointed experts**

• **co-rapp. assessment
by other CAT members**

• **CAT proposal for a decision**

• **CHMP agreement**

• **marketing authorisation granted by the EC**

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- ✓ to provide advice, on whether a product falls within the definition of an advanced therapy medicinal product → **classification**
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Scientific recommendation on advanced therapy classification (art. 17)

(b) to provide advice, pursuant to Article 17, on whether a product falls within the definition of an advanced therapy medicinal product;

- ✓ The CAT will answer the following questions for a given product submitted for classification:
 - Is it a biological ?
 - Is it a medicinal product
 - Is it an ATMP
 - What ATMP ?
- ✓ Within 60 calendar days following receipt of a valid request for scientific recommendation classification, the EMEA with involvement of the CAT, shall deliver its recommendation after consultation with the European Commission (EC).

Tasks of the Committee for Advanced Therapies (art. 23)

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→ **Scientific advice**
- ✓ to assist scientifically in the elaboration of any documents related to the fulfilment of the objectives of this Regulation → criteria and guidelines

http://www.emea.europa.eu/htms/human/raguidelines/sa_pa.htm

- Introduction
- General
- Innovation Task Force (ITF)
- Advanced Therapies
- Paediatrics
- Small and Medium-sized Enterprises (SME)
- Orphans
- Scientific Advice and Protocol Assistance
- Pre-Marketing Authorisation
 - Pre-Submission
 - Dossier Submission Requirements
 - Application & Evaluation
 - Post-Opinion
- Post-Marketing Authorisation
 - General
 - Dossier submission requirements
 - Type I Variations
 - Type II Variations
 - Type II Variations vs Extension applications
 - Extensions
 - New Variation Regulation

Regulatory and procedural guidance

Scientific Advice and Protocol Assistance

D = Draft **A** = Adopted **O** = Overview of Comments **u** = Click on the icon to access document

Title	D	A	O	Reference Number	Document Date
General					
New Framework for Scientific Advice and Protocol Assistance (final)			<u></u>	EMA/267187/2005	26 Apr 2006
EMA Guidance for companies requesting scientific advice or protocol assistance			<u></u>	EMA-H-4260-01	19 Jan 2007
EMA-FDA parallel scientific advice pilot programme: general principles			<u></u>	n/a	22 Jul 2009
Updated template for letter of intent for request of Scientific Advice / Protocol Assistance			<u></u>	n/a	n/a
SAWP meeting dates and submission deadlines (2009)			<u></u>	EMA/CHMP /SAWP/135280/2008	22 May 2009
SAWP meeting dates and submission deadlines (2010)			<u></u>	EMA/CHMP /SAWP/138987/2008	19 Jun 2009
Scientific Advice and Protocol Assistance Procedure			<u></u>	SOP/H/3037	01 Jul 2008
General dealings between SAWP secretariat and working parties, SAGs, committees and patients organisations			<u></u>	WIN/H/3036	01 Jul 2008
Organisation of Scientific Advice Working Party meetings			<u></u>	WIN/H/3195	28 Jul 2008

Tasks of the Committee for Advanced Therapies (art. 23)

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- ✓ to advise on any medicinal product which may require, for the evaluation of its quality, safety or efficacy, expertise in one of the scientific areas
→ Scientific advice
- ✓ to assist scientifically in the elaboration of any documents related to the fulfilment of the objectives of this Regulation → **criteria and guidelines**

New criteria and Guidelines

- ✓ Multidisciplinary approach
- ✓ Specific questions due to the nature of the products (Ethics, methodology, long term follow up, ...)
- ✓ New concept and mechanisms to take onboard
- ✓ Adaptation of the current approaches both for the scientific criteria and production processes

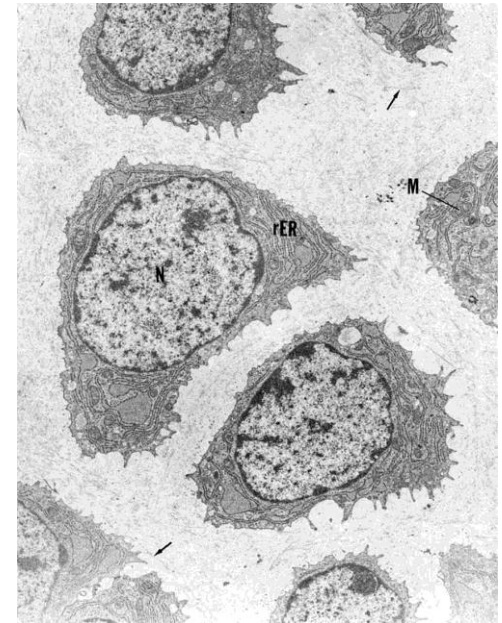
Examples of specific questions

- ✓ Quality
 - Impurities
 - Cells: Culture conditions and their impact on differentiation
 - Bioassay, characterisation and definition of the product
 -
- ✓ Safety
 - tissue cross-reactivity?
 - unwanted biodistribution?
 - toxicity studies: relevance of the experimental models (animal or in silico) ?
- ✓ Efficacy
 - Relevance of the clinical endpoints
 - additional safety measures required?
 - Immunogenicity
 - Long term follow-up
- ✓ Regulatory
 - How to find the correct regulatory routes for guidance documents (e.g. cell-based tumour vaccines)
 - How to deal with products that have already been used without evidence?
 - Regulation of long-term follow-up of efficacy
- ✓ Ethics
 - How to perform first-in-human trials?
 - How to deal e.g. with the risk of insertional mutagenesis?

Challenges with cell-based products

✓ Cells are complex systems

- Cells are dependent on their (micro-)environment
 - Species-specificity
 - Disease-specificity
- Cells are reactive to their environment
- Cell cultures can become heterogeneous
- Cells might de-differentiate (e.g. during longer cell culture)
- Cells might migrate („biodistribution“)
- Cells are fragile and (sometimes) mortal



⇒ Regulatory consequences:

- ✓ Need for adequate characterization
- ✓ but also necessity to accept limitations

Need for a “risk-based” approach

- ✓ The following general risk criteria can be used in the estimation of the overall risk of the product:
- origin (autologous - allogeneic);
 - ability to proliferate and differentiate;
 - ability to initiate an immune response (as target or effector);
 - level of cell manipulation (in vitro/ex vivo expansion / activation / genetic manipulation);
 - mode of administration (ex vivo perfusion, local, systemic);
 - duration of exposure (short to permanent);
 - combination product (cells + bioactive molecules or structural materials)
 - availability of clinical data on or experience with similar products.

Technical Guidances available: Gene therapy

- Quality, Preclinical and Clinical Aspects of Gene Transfer Medicinal Products CPMP/BWP/3088/99 Apr 2001 Oct 2001
- Development and Manufacture of Lentiviral Vectors CHMP/BWP/2458/03
- Non-Clinical testing for Inadvertent Germline transmission of Gene Transfer EMEA/273974/05
- Development of a guideline on the quality, pre-clinical and clinical aspects of medicinal products containing genetically modified cells CHMP/GTWP/405681/06
- Non-clinical studies required before first clinical use of gene therapy medicinal products CHMP/GTWP/125459/06
- Scientific Requirements for the Environmental Risk Assessment of Gene Therapy Medicinal Products CHMP/GTWP/125491/06
- Environmental Risk Assessments for Medicinal Products containing, or consisting of, Genetically Modified Organisms (GMOs) (EMEA/CHMP/473191/06)
- Quality, non-clinical and clinical issues relating specifically to recombinant adeno-associated viral vectors CHMP/GTWP/587488/07
- Follow-up of patients administered with gene therapy medicinal products CHMP/GTWP/60436/07
- ICH Oncolytic Viruses CHMP/GTWP/607698/08
- ICH General Principles to Address Virus and Vector Shedding CHMP/ICH/449035/09

www.emea.europa.eu/htms/human/humanguidelines/biologicals.htm

Technical Guidances available: Cell therapy

- Human cell-based medicinal products CHMP/410869/06
- Points to Consider on Xenogeneic Cell Therapy CHMP/1199/02
- Potency testing of cell based immunotherapy medicinal products for the treatment of cancer CHMP/BWP/271475/06
- Revision of the Points to Consider on Xenogeneic Cell Therapy Medicinal Products CHMP/165085/07
- Xenogeneic Cell-based medicinal products CHMP/CPWP/83508/09
- Reflection paper on *In-Vitro* cultured chondrocyte containing products for cartilage repair of the knee CAT/CPWP/288934/09

www.emea.europa.eu/htms/human/humanguidelines/biologicals.htm

Certification of quality and non-clinical data (art. 18)

- ✓ Specific provision in the ATMP regulation (recital 25 and article 18)
- ✓ Incentive measure for small and medium-sized enterprises developing an advanced therapy medicinal product.
- ✓ submission to the Agency all relevant quality and, where available, non-clinical data required in accordance with modules 3 and 4 of Annex I to Directive 2001/83/EC, for scientific evaluation and certification.
- ✓ Specific

COMMISSION REGULATION (EC) No 668/2009
of 24 July 2009

implementing Regulation (EC) No 1394/2007 of the European Parliament and of the Council with regard to the evaluation and certification of quality and non-clinical data relating to advanced therapy medicinal products developed by micro, small and medium-sized enterprises

Objective of Certification Procedure

- ✓ Stand alone evaluation procedure
- ✓ Not directly binding for future MAA or Clinical trial application (CTA): Certificate will not replace any data to be submitted in MAA or CTA
- ✓ No Assessment of benefit/risk
- ✓ No Statements on appropriateness to enter into clinical trials
- ✓ No Prospective statements pertaining to the further development of the product: that is the role of Scientific Advice

http://www.emea.europa.eu/htms/human/advanced_therapies/certification.htm

Certification procedure

Introduction

Advanced Therapies Regulation

Regulatory and Procedural Guidance

Special procedures designed for ATMPs

ATMP Classification

Certification Procedure

Scientific guidelines

How to get support from the EMA

Interested parties

See also:

Committee for Advanced Therapies

AT Monthly Report

Contact Point

Questions relating specifically to the authorisation of advanced therapy medicinal products may be submitted to: AdvancedTherapies@emea.europa.eu

The certification procedure is one of the new procedures provided for Advanced Therapy Medicinal Products (ATMPs) in the Regulation on Advanced Therapies (Article 18 of Regulation (EC) No 1394/2007). [Commission Regulation \(EC\) No 668/2009](#) provides for implementing provisions for the certification procedure.

The certification procedure is the scientific evaluation by the CAT of quality and (where available) non-clinical data for ATMPs under development by Small and Medium-sized Enterprises (SMEs). Further to the scientific evaluation, EMEA will issue a certificate. A 90-day procedure has been developed for the evaluation and certification.

For more information on the procedure for certification and on the content of an application for ATMP certification, please consult following documents:

- [Procedural advice on the Certification of quality and non-clinical data for small and medium-sized enterprises developing advanced therapy medicinal products](#) (corr. 1 (23/09/09))
- [Scientific Guideline on the minimum quality and non-clinical data for certification of advanced therapy medicinal products](#) (corr. 1 (23/09/09))

Templates for the letter of intent to submit an application for ATMP certification and for the certification application form will be published shortly.

SMEs planning to submit an application for certification in the next months should contact

Conclusions

- ✓ Tissues and cells [engineered] products: two possible regulatory status in Europe, medicinal products or not
- ✓ New « advanced » products are now classified as medicinal products by EU regulation:
 - European centralised procedure for their authorisation prior marketing
 - European Scientific committee dedicated for their evaluation and proposal for authorisation
- ✓ For Tissues or Cells products, which are not classified as ATMP, considering their characteristics, not only in terms of benefit but also in terms of potential risk, it is important to regulate them, so that the patients, in the EU community, are offered reliable products and services.
 - EU Directive foresees the contribution of the National competent authorities at the various stages of the life cycle of those products

Acknowledgment

✓ Afssaps

- Sandrine Jacob
- Dominique Labbé
- Sophie Lucas
- Pierrette Zorzi

✓ EMEA

- Patrick Celis
- Lucia d'Apote
- Veronika Jekerle
- Elisa Pedone
- Marie-Hélène Pinheiro
- Christian Schneider (CAT Chair)
- Paula Salmikangas (CAT Vice Chair)