1st Workshop on Advance Therapy Medicinal Products (ATMPs)

Scientific Recommendation on the Classification of ATMPs

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EMEA
Regulatory Affairs

AGENDA

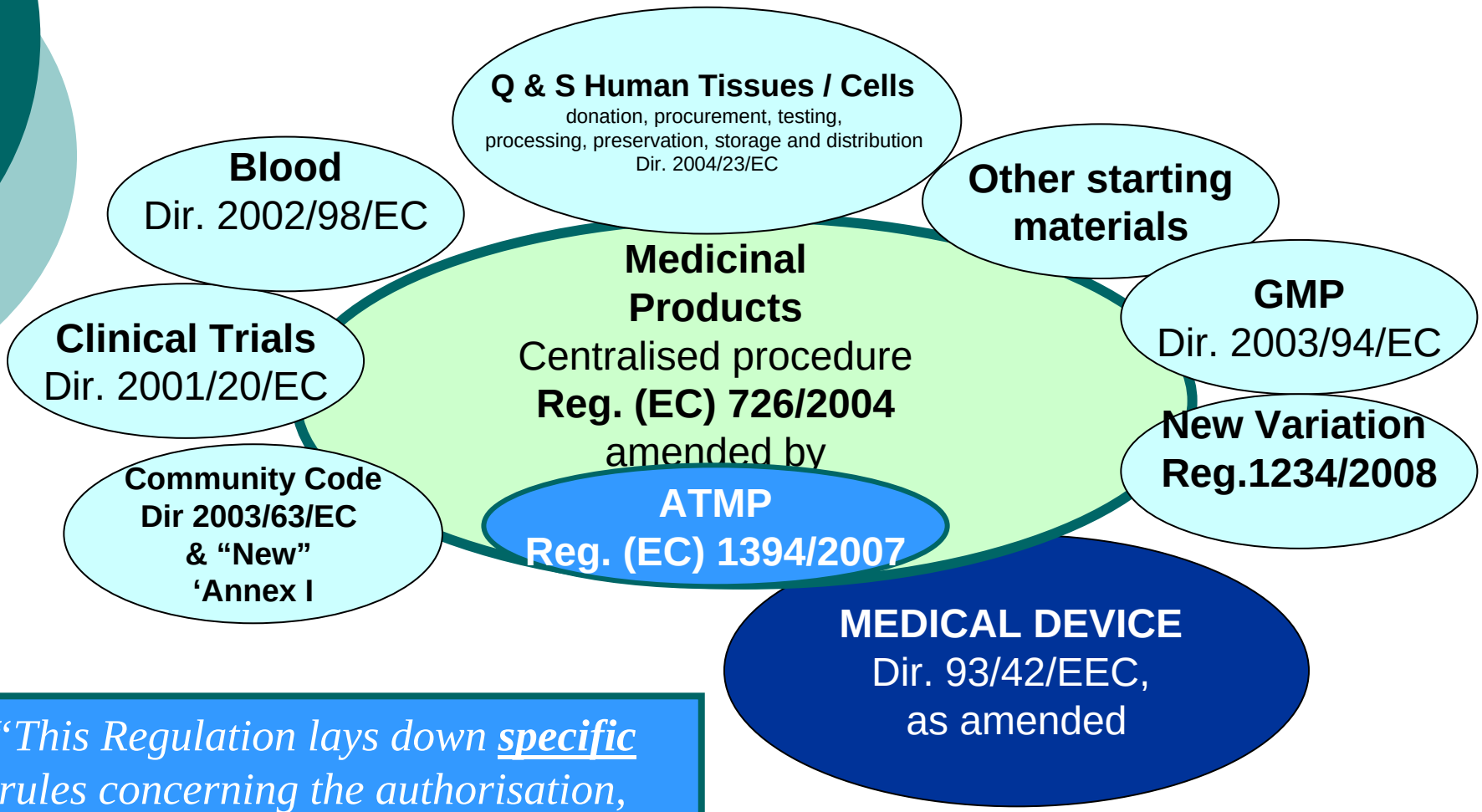
Introduction

1. **ATMPs Definition**
2. **Borderlines' considerations**
3. **Scientific Recommendation**
   - 3.1 Legal basis
   - 3.2 Procedure
   - 3.3 Role and Responsibilities
   - 3.4 Timetable
   - 3.5 Decision Tree
   - 3.6 Publication of Summaries
   - 3.7 Timing of Request for Scientific Recommendation of Classification

Conclusion

INTRODUCTION

ATMPs LEGISLATIVE REFERENCES



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

1. ATMP DEFINITION

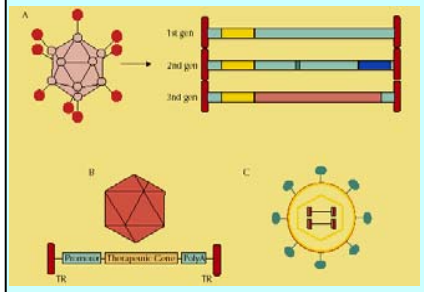
ADVANCE THERAPY MEDICINAL PRODUCTS

Gene therapy medicinal products

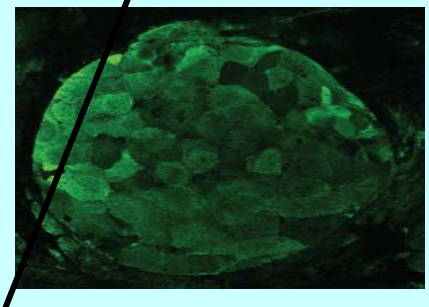
Somatic cell therapy medicinal products

Tissue engineering products

Genetically modified cells

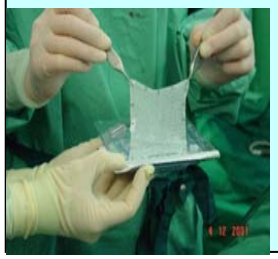


www.heartandmetabolism.org



Nat Biotechnol 2005, 23(7)

www.biomed.brown.edu



COMBINED ATMP + MEDICAL DEVICES

Source: Dr Christian Schneider, CAT Chairman

1. ATMP DEFINITION:
GENE THERAPY MEDICINAL PRODUCT

NEW DEFINITION
ANNEX 1 Dir. 2001/83/EC

JUST PUBLISHED

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.

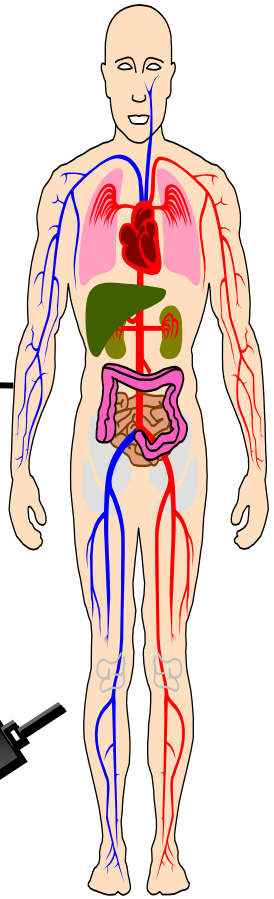
Gene therapy medicinal products shall not include vaccines against infectious diseases.

1. ATMP DEFINITION:
GENE THERAPY MEDICINAL PRODUCT

GENETICALLY MODIFIED HUMAN CELLS

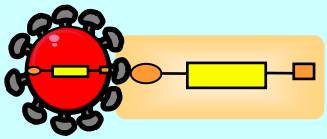
VECTOR, NUCLEIC ACIDS, REPLICATING MICRO-ORGANISM (NOT INCL. LIVE VACCINES)

cell line → **cell**

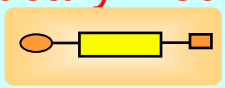


1) Isolation of the target cells

2) Gene transfer

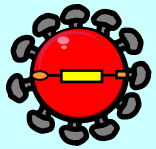


3) Re-Infusion of the genetically modified cells

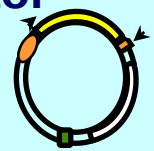


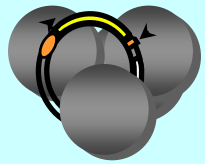
Direct application:

- **viral vector**

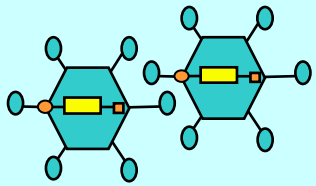


- **non-viral vector**





- **naked DNA**
- **replicating rec. micro-organism (adenovirus, salmonella)**



Source: Prof. K. Cichuteck- GTWP Chairman

1. ATMP DEFINITION:

SOMATIC CELL THERAPY MEDICINAL PRODUCT

JUST PUBLISHED

NEW DEFINITION ANNEX 1 Dir. 2001/83/EC

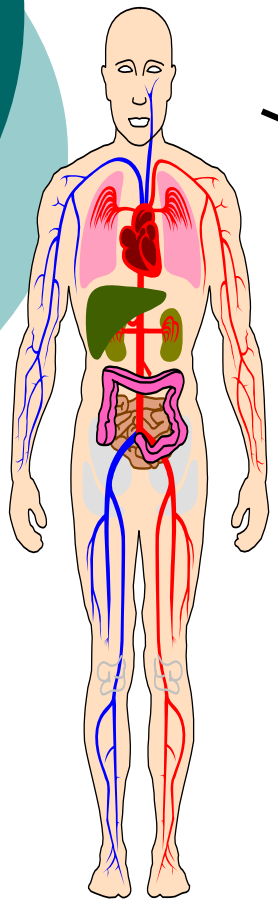
Somatic cell therapy medicinal product means a biological medicinal product which has the following characteristics:

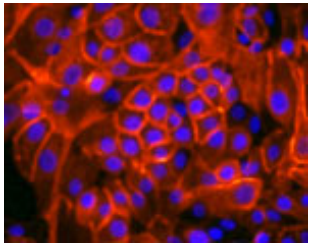
(a) contains or consists of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor;

(b) is presented as having properties for, or 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 its cells or tissues.

For the purposes of point (a), the manipulations listed in Annex I to Regulation (EC) No 1394/2007, in particular, shall not be considered as substantial manipulations.

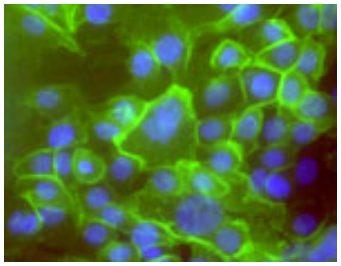
1. ATMP DEFINITION:
SOMATIC CELL THERAPY MEDICINAL PRODUCT





AUTOLOGOUS
or
ALLOGENIC CELLS

- **ADULT CELLS**: AUTOLOGOUS OR ALLOGENEIC
- **ADULT MULTIPOTENT STEM CELLS**
- **INDUCED PLURIPOTENT STEM CELLS (NEW)**
- **CORD BLOOD STEM CELLS**
- **EMBRYONIC STEM CELLS**



XENOGENIC CELLS

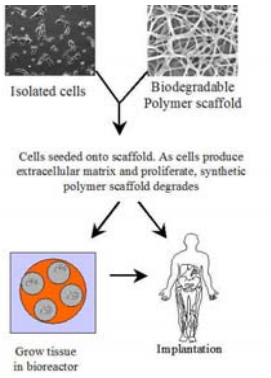
CELL PROCESSING and GRAFT SEEDING

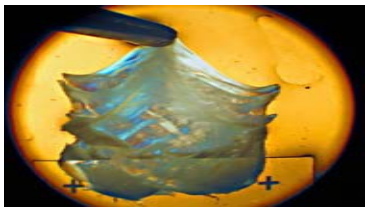
GRAFT IMPLANTATION

1. ATMP DEFINITION:
TISSUE ENGENEERED MEDICINAL PRODUCT

NEW DEFINITION Art. Reg. 1394/2007

- **Tissue Engineered products** (TEP)
  - Contain/consist of engineered cells/tissues
  - 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
    - Examples:
      - Artificial skin (burn wounds)
      - Neo-organs (corneal, blood vessel, liver, cartillage or bone tissue engeneereing)





2. BORDERLINE CONSIDERATIONS

SOME INCLUSION/EXCLUSION CRITERIA & PRINCIPALS (1)

- **TEP** may contain:
  - Non viable and viable cells are included
  - Products which **do not** contain any **viable cells** and which **do not** act principally by metabolic action are excluded
- Cell/device association no longer considered *a priori* as 'engineered'
  - Aspect/definition of « substantial manipulation » to be considered

2. BORDERLINE CONSIDERATIONS

SOME INCLUSION/EXCLUSION CRITERIA & PRINCIPALS (2)

- In case ATMP containing **both autologus** and **allogenic** cells or tissues it shall be considered to be for **allogenic use**
- In case product falls in definition of **TEP and sCT** it shall be considered as **TEP**
- In case products falls in definition of **GT and TEP** or **sCT,** then **GT > TEP > sCT**

2. BORDERLINE CONSIDERATIONS

SOME EXCLUSION CRITERIA AND PRINCIPALS (3) ART. 28 OF REG. 1394/2007 SO CALLED "HOSPITAL EXEMPTION"

- Additional exclusion under very specific conditions e.g.:
  - Non-routine basis of production
  - Specific quality standards
  - Used in same MS in hospital (manufacturing authorised by Comp. Authority of MS)
  - Custom-made product for individual patient
  - Under the exclusive professional responsablity of a practitioner

→ National rules on the use of cells on ethical grounds

3. SCIENTIFIC RECOMMENDATION

3.1 LEGAL BASIS: Art. 17 OF Reg.(EC) NO 1394/2007

*"1. Any applicant developing a product based on genes, cells or tissues **may** request a scientific recommendation of the Agency with a view to **determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product.** The Agency shall deliver this recommendation after consultation with the **Commission** and **within 60 days** after receipt of the request.*

*2. The Agency shall **publish summaries** of the recommendations delivered in accordance with paragraph 1, **after deletion of all information of commercial confidential nature."***

3. SCIENTIFIC RECOMMENDATION

3.2 PROCEDURE

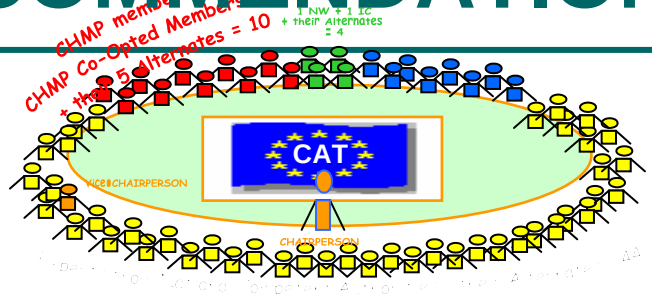
Letter of Intent

Request Form

- ❑ Company's Information
- ❑ Product Information:
  - ✓ Scientific Aspect
  - ✓Legal/Regulatory Aspects
  - ✓RA Status& Current Medical Use
  - ✓Other Info
  - ✓Position of Company on Product's Classification

CAT Secretariat

ITF: Nomination EMEA Coordinator



EMEA Briefing Note

Appoint of CAT Coordinator

Report

- ❑ Product Information
- ❑ Summary for Public Release
- ❑ Applicant's position on RA classification
- ❑ EMEA/CAT Comments
- ❑ EMEA/CAT Conclusions

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

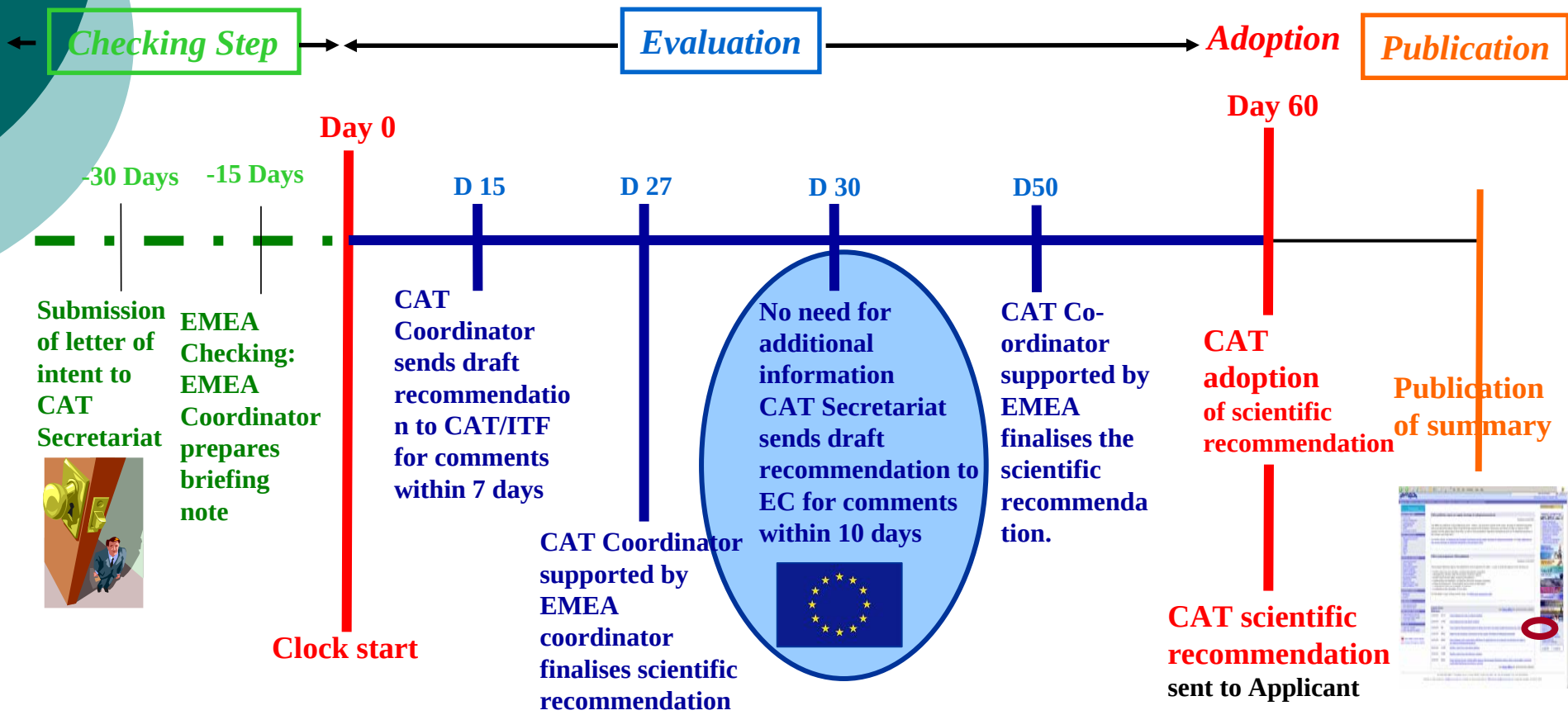
3. SCIENTIFIC RECOMMENDATION

3.3 ROLES AND RESPONSIBILITIES

- **CAT:**
  - responsible for provision of scientific recommendations
- **CAT Secretariat**
  - coordinates the procedure at the level of the CAT
- **CAT Coordinator(s)**
  - prepare and finalise the scientific recommendations
  - identify need to consult NB and/or WP for agreement at CAT
- **EMEA Coordinator**
  - Contact point
  - check adequacy of requests
  - Support CAT Coordinator
- **Innovation Task Force (ITF)**
  - peer-review including regulatory, legal and scientific aspects

3. SCIENTIFIC RECOMMENDATION

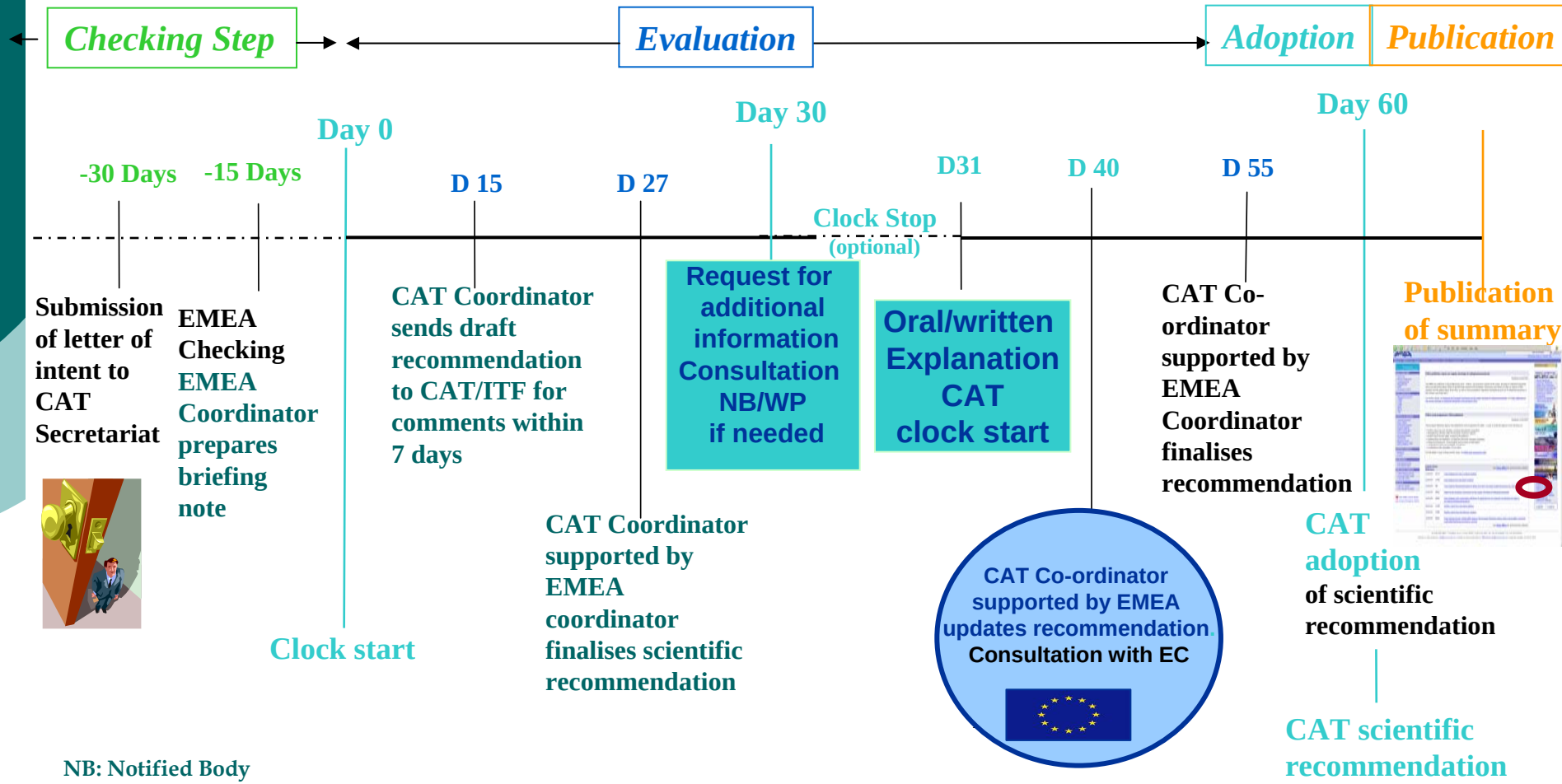
3.4 TIMETABLE (standard)



EC: European Commission

3. SCIENTIFIC RECOMMENDATION

3.4 TIMETABLE (when additional information is requested)

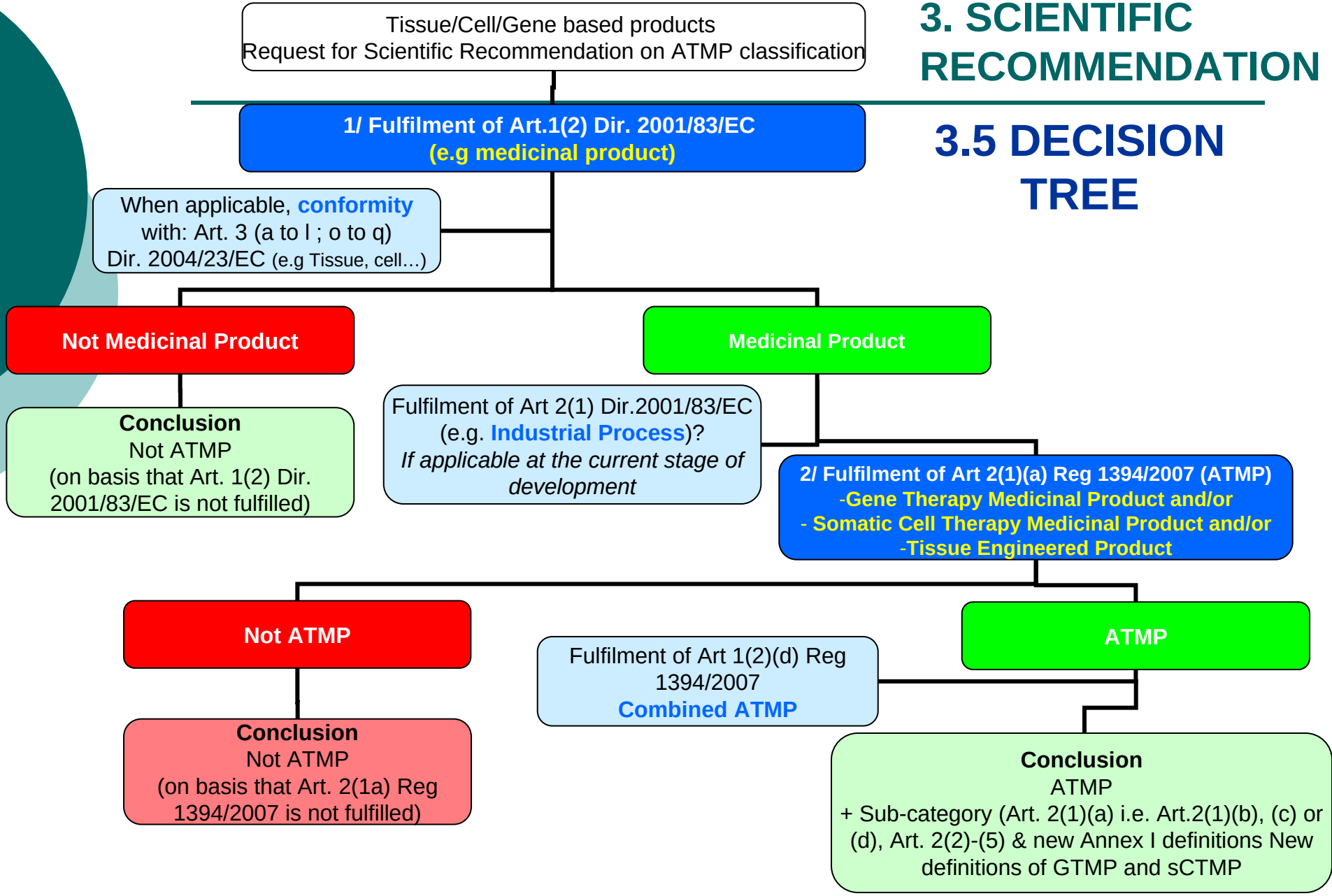


NB: Notified Body

WP: Working Party

3. SCIENTIFIC RECOMMENDATION

3.5 DECISION TREE



3. SCIENTIFIC RECOMMENDATION

3.6 TRANSPARENCY: SUMMARY REPORT

- **Follow the transparency rules**
- **Removal of confidential information**
- **Summary will contain the following information:**
  - Product description
  - Therapeutic area
  - Outcome of the scientific recommendation
  - Date

Reference : **Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents (EMEA/45422/2006): http://www.emea.europa.eu/pdfs/human/euleg/4542206en.pdf**

3. SCIENTIFIC RECOMMENDATION

3.6 TRANSPARENCY

6. Proposed Summary for future publication

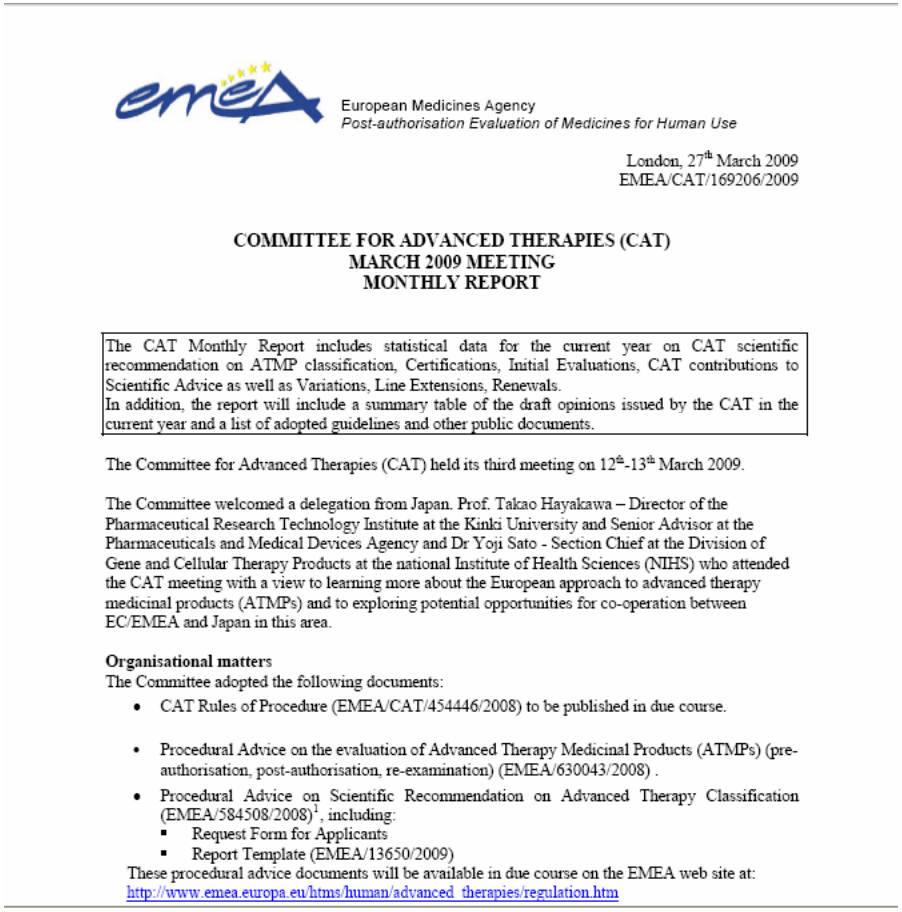
Product description	
Therapeutic area	
Outcome of the scientific recommendation	
Date	

Templates Request/Report Form

Applicant include proposed information for publication

3. SCIENTIFIC RECOMMENDATION

3.6 TRANSPARENCY: CAT MONTHLY REPORT



European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 27th March 2009
EMEA/CAT/169206/2009

COMMITTEE FOR ADVANCED THERAPIES (CAT)
MARCH 2009 MEETING
MONTHLY REPORT

The CAT Monthly Report includes statistical data for the current year on CAT scientific recommendation on ATMP classification, Certifications, Initial Evaluations, CAT contributions to Scientific Advice as well as Variations, Line Extensions, Renewals.
In addition, the report will include a summary table of the draft opinions issued by the CAT in the current year and a list of adopted guidelines and other public documents.

The Committee for Advanced Therapies (CAT) held its third meeting on 12th-13th March 2009.

The Committee welcomed a delegation from Japan. Prof. Takao Hayakawa – Director of the Pharmaceutical Research Technology Institute at the Kinki University and Senior Advisor at the Pharmaceuticals and Medical Devices Agency and Dr Yoji Sato - Section Chief at the Division of Gene and Cellular Therapy Products at the national Institute of Health Sciences (NIHS) who attended the CAT meeting with a view to learning more about the European approach to advanced therapy medicinal products (ATMPs) and to exploring potential opportunities for co-operation between EC/EMEA and Japan in this area.

Organisational matters
The Committee adopted the following documents:

- CAT Rules of Procedure (EMEA/CAT/454446/2008) to be published in due course.
- Procedural Advice on the evaluation of Advanced Therapy Medicinal Products (ATMPs) (pre-authorisation, post-authorisation, re-examination) (EMEA/630043/2008) .
- Procedural Advice on Scientific Recommendation on Advanced Therapy Classification (EMEA/584508/2008)[1], including:
  - Request Form for Applicants
  - Report Template (EMEA/13650/2009)

These procedural advice documents will be available in due course on the EMEA web site at:
http://www.emea.europa.eu/htms/human/advanced_therapies/regulation.htm

3. SCIENTIFIC RECOMMENDATION

3.6 TRANSPARENCY: CAT MONTHLY REPORT

INITIAL EVALUATION ATMP MAAs

SCIENTIFIC RECOMMENDATION

CONTRIBUTION TO SCIENTIFIC ADVICE

CERTIFICATION

- Products legally on the Community market in accordance with national or Community legislation that need to comply with Regulation 1394/2007 by end of 2011/2012 (Article 29 of Regulation (EC) No 1394/2007[2]). CAT stressed the importance of early contacts with the Agency (see procedural announcement below).
- CAT members provided feedback on the implementation of the Article 28 (2) of Regulation (EC) No 1394/2007 ('hospital exemption' clause) at Member State level.

General scientific issues

The Committee discussed:

- Requirements for chondrocyte-containing products
- A proposal to strengthen collaboration with academia, including the publication of an overview article in a scientific journal on the role of the CAT and on challenges with ATMPs.
- Risk management plans and post-authorisation follow-up of ATMPs and the impact on evaluation procedures (pre /post activities).

Product-related activities

The Committee discussed ongoing evaluation procedures for ATMPs and other related procedures as summarised in the following tables.

Initial Evaluation of MAA for ATMP		
	2009	Total
Submitted	3	3
Ongoing	3	3
Positive draft Opinion	0	0
Negative draft Opinion	0	0
Withdrawals	0	0

Scientific recommendation on advanced therapy classification		
	2009	Total
Submitted	0	0

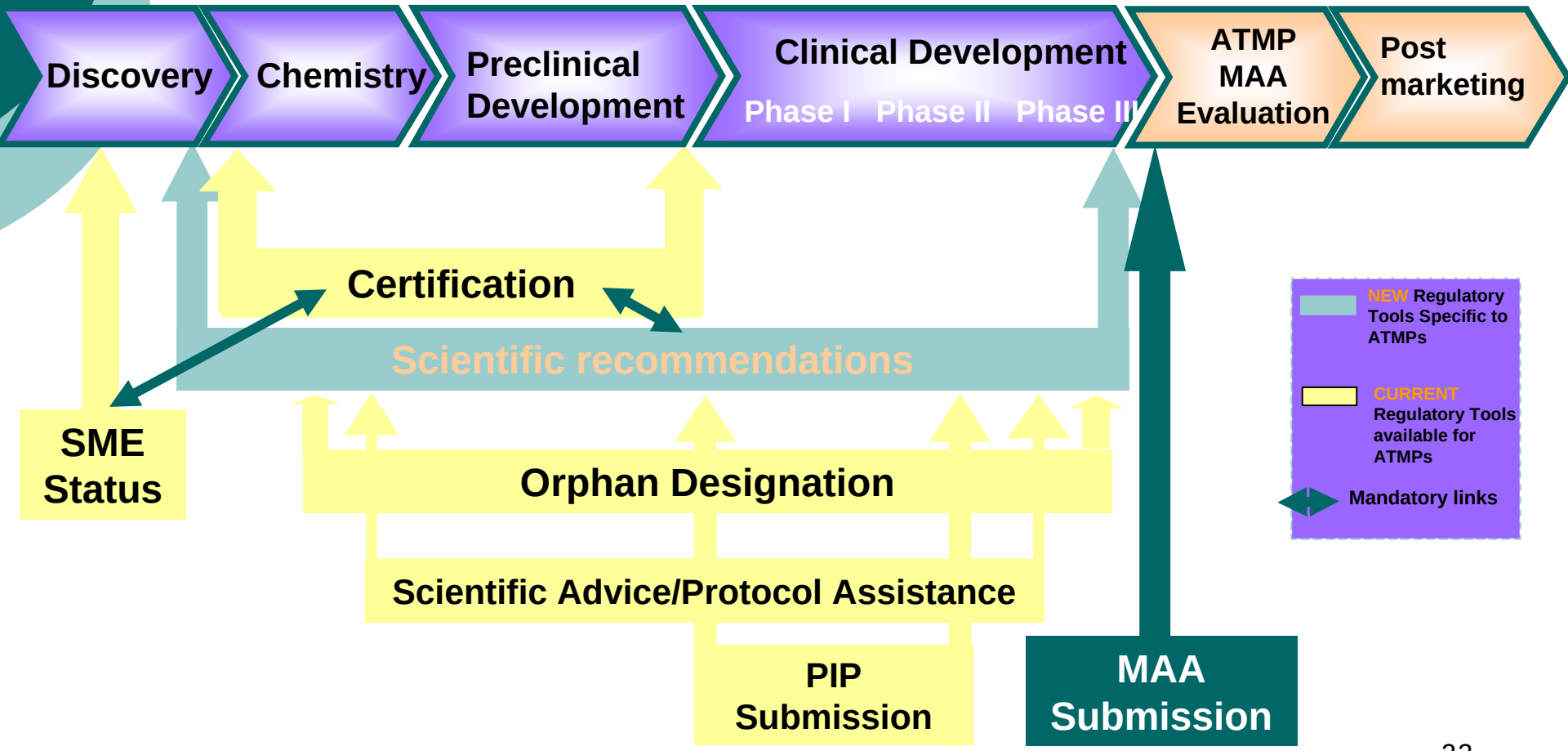
Contribution to scientific advice procedures		
	2009	Total
Submitted	5	5

Certification of quality and non-clinical data for small and medium-sized enterprises developing ATMPs		
	2009	Total
Submitted	0	0

3. SCIENTIFIC RECOMMENDATION

3.7 TIMING of REQUEST

ATMP DRUG DEVELOPMENT



CONCLUSION

PROCEDURE PRINCIPALS (1)

- **Optional procedure**
- **Systematic consultation with EC/ Optional consultation Notified Bodies (NB) or Working Parties (WP)**
- **Entry door**
  - CAT Secretariat:
    AdvancedTherapies @emea.europa.eu
  - ATMP Web Page:
    http://www.emea.europa.eu/htms/human/advanced_therapies/intro.htm

- **Procedural Guideline & Templates** (shortly)**available on Web**

CONCLUSION

PROCEDURE PRINCIPALS (2)

Discussion platforms :

- **EMEA Innovation Task Force (ITF)**
  Briefing meetings with possible participation of CAT Members
  (informal discussion - Early dialogue to proactively identify scientific, legal and regulatory issues and to clarify regulatory options opened such as classification)

- Possible oral explantation in front of CAT at Day 31 of procedure (formal discussion)

- **No fees**

- **Publication of Summaries of Recommendations**

Thank you for your attention

European Medicines Agency

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ANY QUESTION ?