1st Workshop on Advance Therapy Medicinal Products (ATMPs)

Overview of the Procedure and interactions between CAT and CHMP

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EMEA
Regulatory Affairs

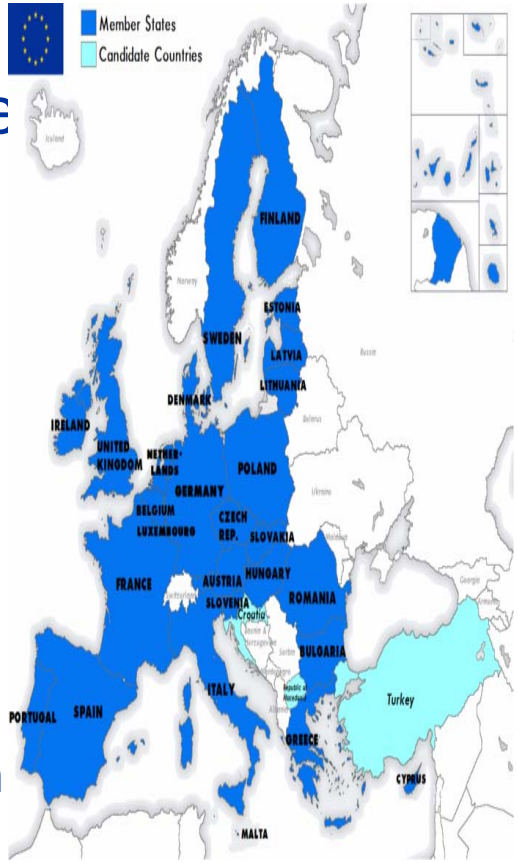
AGENDA

1. Expansion of mandatory scope of the Centralised Procedure by ATMPs
2. Rapporteurs appointment
3. CAT-CHMP Assessment Teams
4. ATMP Evaluation procedure
5. Re-examination procedure
6. Withdrawal
7. Post-Authorisation activities
8. Transparency

1. Expansion Of Mandatory Scope Of The Centralised Procedure By ATMPs

REGULATIONS (EC) NO 726/2004 AND NO 1394/2007

- Regulation (EC) No 726/2007 legal basis for the EMEA Centralise :
  - **1 evaluation and Marketing Authorisation** valid EU
  - **1 Invented name (Tradename)**
  - **1 Common Labelling** (22 languages identical)
    - **Summary of Product Characteristics (SPC)**
    - **User Package Leaflet & Package Labelling**
  - **Maximum time limit:** 210 days Evaluation ---> Opinion

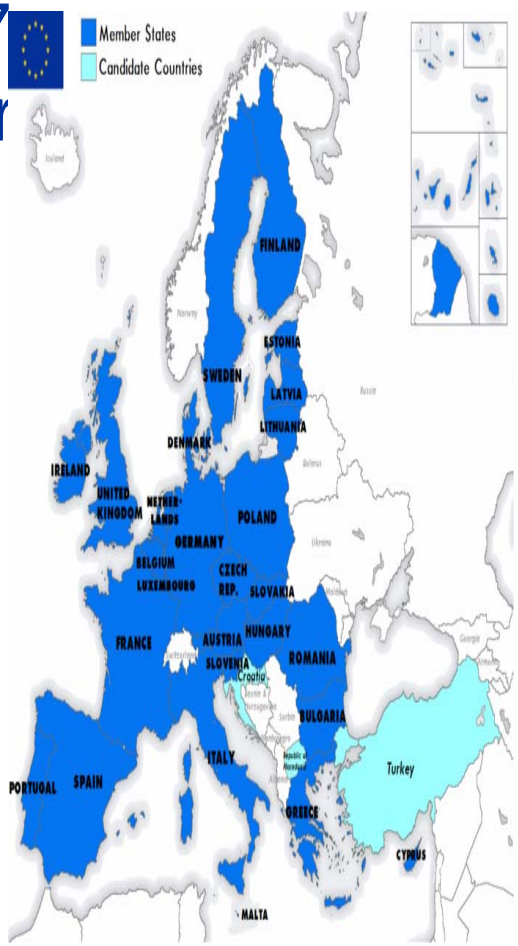


1. Expansion Of Mandatory Scope Of The Centralised Procedure By ATMPs

REGULATIONS (EC) NO 726/2004 AND NO 1394/2007

Regulation (EC) No 1394/2007 made the Centralised procedur mandatory for ATMP :

- **Pooling of Community expertise**
- **Harmonised requirements & evaluation**
- **Ensure uniform and direct access to market**
- **Principles of existing legislation on medicines apply to advanced therapies i.e.**
  - Quality, Safety & Efficacy
  - Marketing authorisation
  - Post-authorisation vigilance



1. Expansion of Mandatory Scope Of The Centralised Procedure By ATMPs

ARTICLE 3(1) OF REGULATION 726/2004

ADVANCE THERAPY MEDICINAL PRODUCTS:

-Gene therapy products

Auto-immune disease and Other immune dysfunctions

- Somatic Cell therapy products

AIDS

Cancer

Neurodegenerative disorder

- Tissue engineered products

Viral diseases

-Recombinant DNA technology
-Controlled gene expression
-Monoclonal AB

Reg. 2309/93

Diabetes

Orphan med. products

Reg. 726/2004

Reg. 1394/2007

Since 1 Jan 95

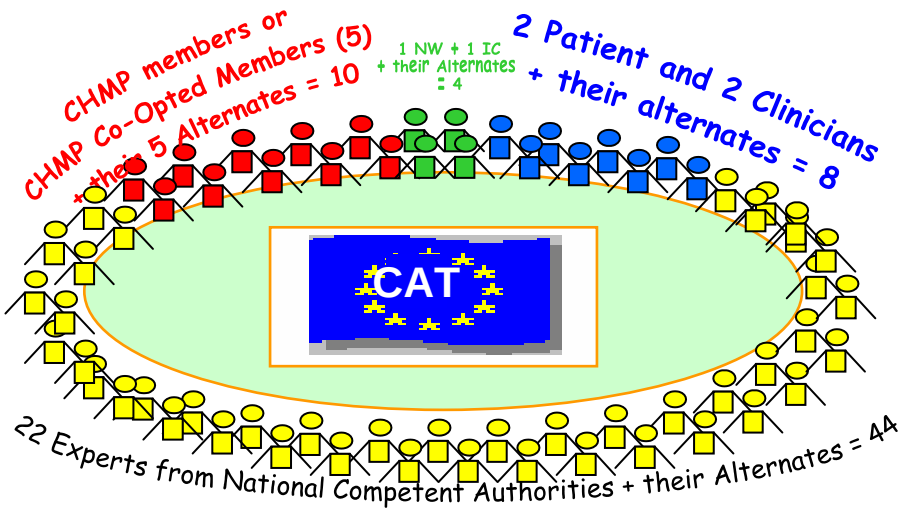
From 20 Nov 05

From 1 May 08

From 30 Dec. 08

2. RAPPORTEUR APPOINTMENT

- This scientific evaluation of ATMPs is to be done primarily by the CAT, which has been established by Regulation (EC) No 1394/2007

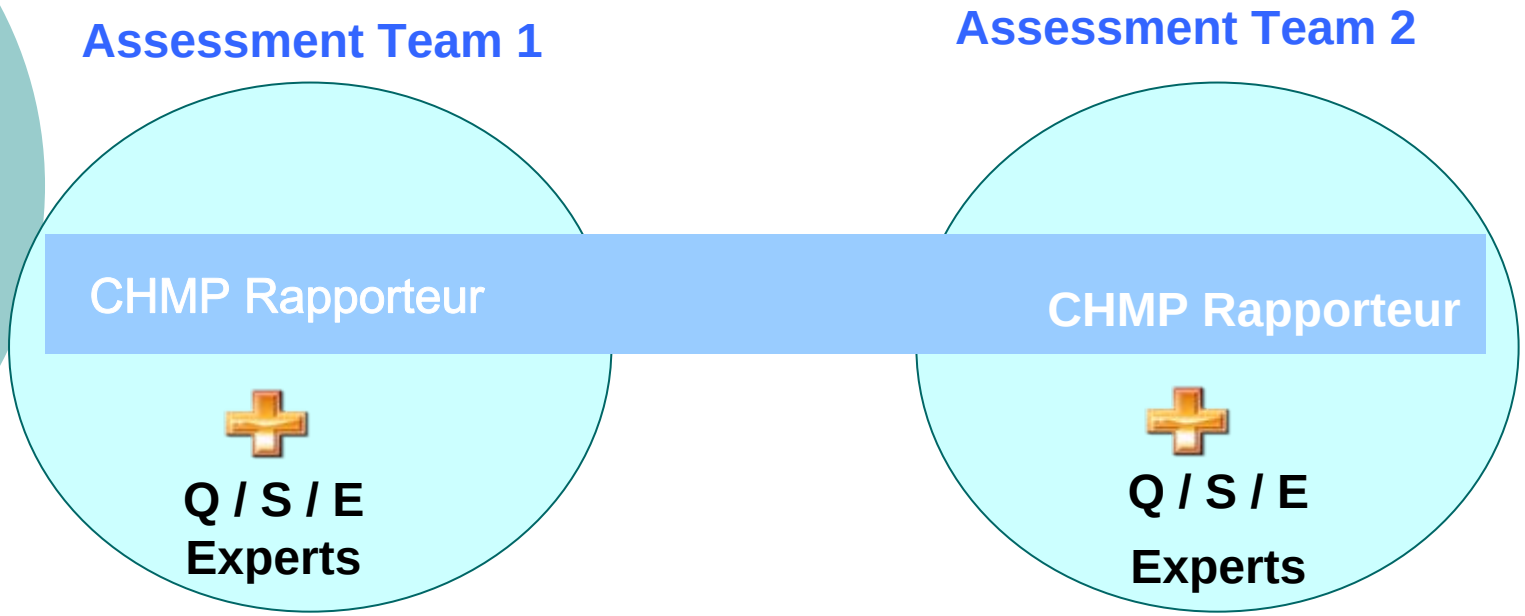


- ATMP Regulation refers to Art 61 (2) of Regulation (EC) No 726/2004:

➡ Rapporteurs appointed at CHMP level

3. CAT-CHMP ASSESSMENT TEAMS

- Assessment teams for « standard » products



"For any scientific evaluation in respect of a procedure a rapporteur shall be appointed from amongst the members of the Committee or alternates. The appointment of the rapporteur shall be made on the basis of ***objective criteria****, which will allow the use of the* ***best available expertise*** *in the EU on the relevant scientific area."*

Reference document: CHMP RAPPORTEUR/CO-RAPPORTEUR APPOINTMENT: PRINCIPLES, OBJECTIVE CRITERIA and METHODOLOGY (EMEA/124066/2005)

3. CAT-CHMP ASSESSMENT TEAMS

- Two extended assessment teams responsible for review of ATMP MAA

Assessment Team 1

CAT Rapporteur

CHMP Co-ordinator

Q/S/E/Phvg/ERA (ATMPs) experts

Assessment Team 2

CAT Co-Rapporteur

CHMP Co-ordinator

Q/S/E/Phvg/ERA (ATMPs) experts

3. CAT-CHMP ASSESSMENT TEAMS

ASSESMENT TEAM 1

ASSESMENT TEAM 2

CAT Rapporteur

CAT Co-Rapporteur

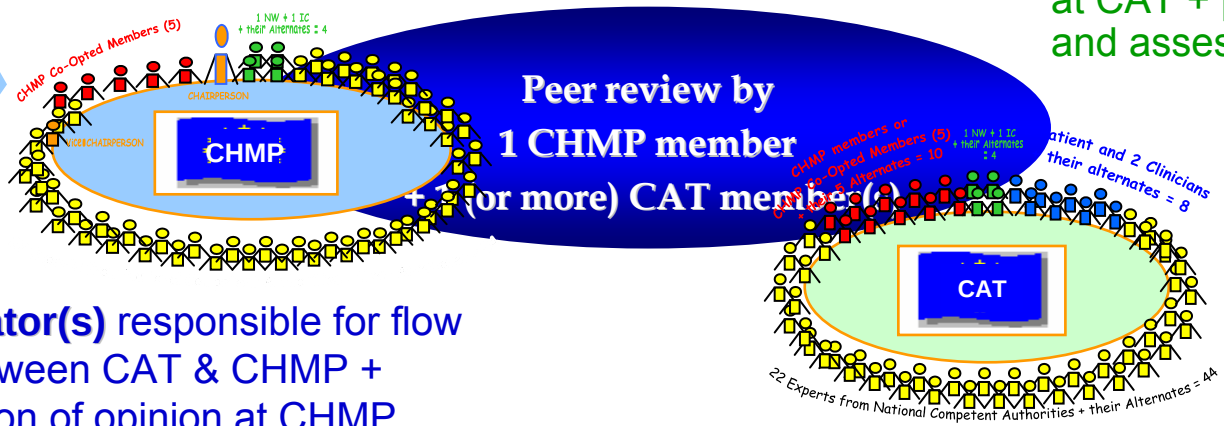
CHMP Co-ordinator

CHMP Co-ordinator

Q/S/E/Phvg/ERA (ATMPs) experts

Q/S/E/Phvg/ERA (ATMPs) experts

CAT (Co)Rapp coordinate procedure & discussions at CAT + prepare draft opinions and assessment reports



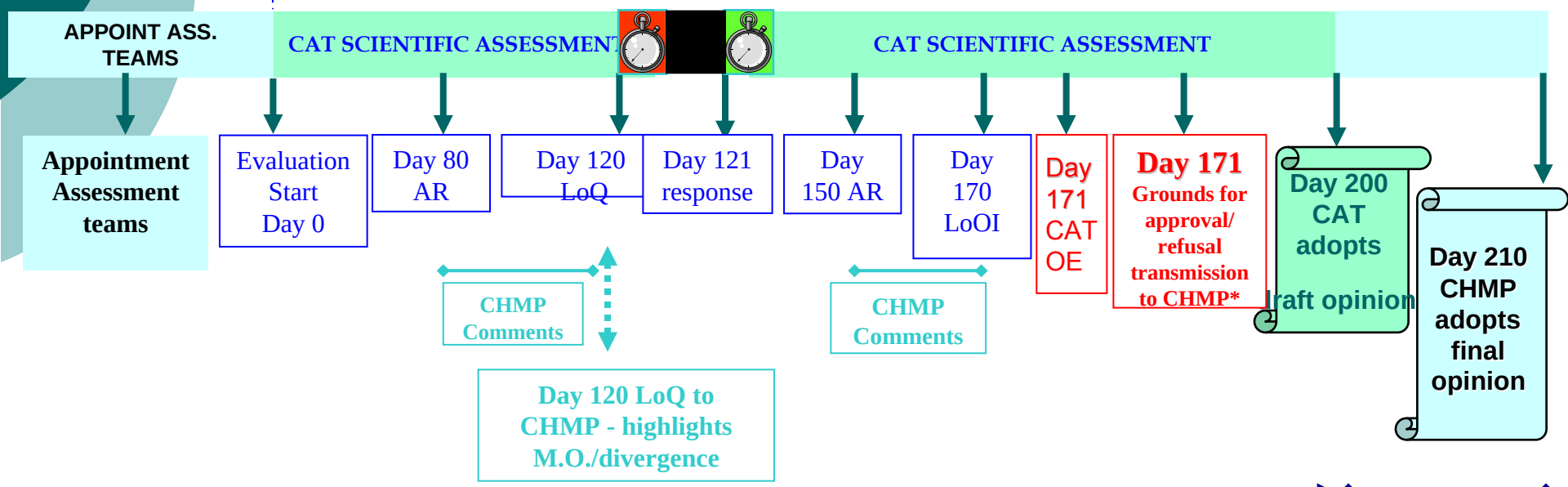
CHMP Co-ordinator(s) responsible for flow of information between CAT & CHMP + discussion/adoption of opinion at CHMP

4. ATMP EVALUATION

CAT
* **Scientific Assessment** (incl. Day 80/150 AR, Adoption LoQ, LoOI)
* Adopt **draft opinion** (Day 182)

CHMP
* **Appoint Rapporteur** [Art. 62(1) Reg. 726/2004]

* **Adopt FINAL CHMP opinion** (by 210 Days)



CHMP INTERACTION with CAT

* Day 180
CHMP discussion on grounds for approval/refusal

** Day 210 CHMP discussion and decision on need for adoption of a LoOI and/or an oral explanation

4. ATMP EVALUATION

ROLE OF THE CAT

- CAT:
  - Adopts the LoQ, LoOI, draft opinion
  - Oral explanation at the CAT
  - Agrees on the need to consult WP/SAG/NB/Inspections

- CAT (Co)-Rapporteurs:
  - Lead the scientific evaluation and discussion at CAT
  - Prepare AR, LoQ, joint AR, LoOI
  - Identify need to consult WP/SAG/NB/Inspections

4. ATMP EVALUATION

ROLE OF THE CHMP

- CHMP
  - Appoint the 2 evaluation teams
  - Peer reviewer through the procedure
  - CHMP comments through the procedure
  - Is informed during its plenary meetings of the key ATMPs scientific issues and divergences
  - Can adopt LoOI and have OE at CHMP at D210
  - Adopt CHMP opinion

- CHMP Co-ordinators
  - Ensure flow of information to CHMP, guide final CHMP discussion when adoption of CHMP opinion
  - Make comments on the milestone documents
  - Identify need to consult WP/SAG/NB/Inspections before D120 (CHMP comments phase D80-D100)

4. ATMP EVALUATION

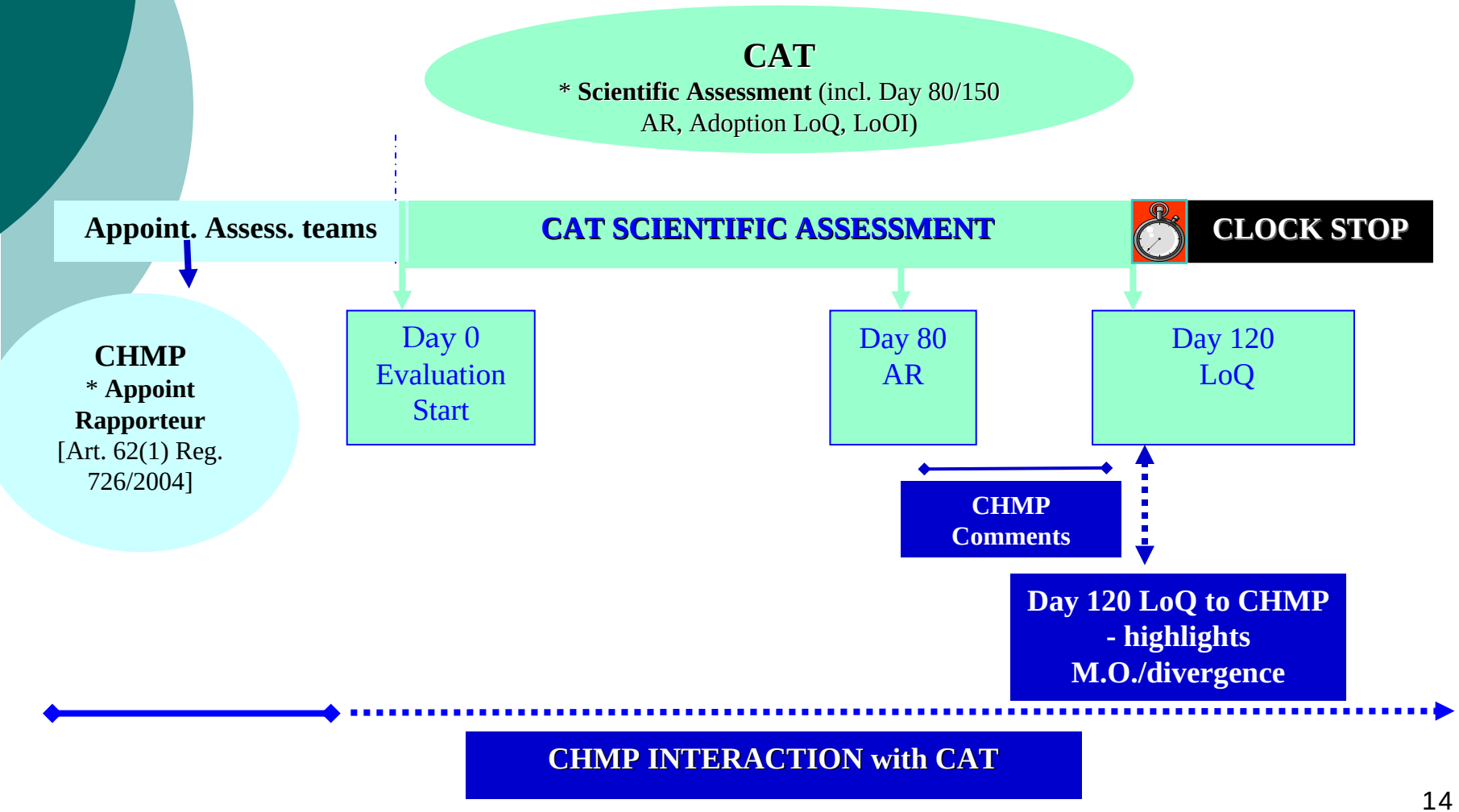
ROLE OF THE EMEA

- The role of the EMEA is to ensure:
  - draft opinion of the CAT is given within 200 days;
  - opinion of the CHMP is given within 210 days;
  - full transparency of the evaluation towards the CAT and the CHMP.

- The EMEA Secretariat prepares:
  - AR on the basis of CAT's (Co)-Rapporteur(s)' AR ensuring scientific and regulatory consistency;
  - draft opinions for transmission and final approval by CHMP;
  - and communicates relevant public information related to the outcome of the assessment of ATMPs and withdrawal.

4. ATMP EVALUATION

ATMP CENTRAL EVALUATION – 1st PHASE



4. ATMP EVALUATION

ATMP CENTRAL EVALUATION – 2d PHASE

Restart of the clock

CAT

* **Scientific Assessment** (incl. Day 80/150 AR, Adoption LoQ, LoOI)

CAT SCIENTIFIC — **CAT O.E.** — **ASSESSMENT**

Day 121 responses

Day 150 AR

Day 170 LoOI

Day 171 CAT O.E.

Day 171 Identification of Grounds for approval/refusal transmission to CHMP*

Day 200 CAT adopts draft opinion

Day 210 CHMP adopts final opinion**

CHMP Comments

LoOI to CHMP - highlight M.O/ /divergences.

CHMP INTERACTION with CAT

* Day 180
CHMP discussion on grounds for approval/refusal

** Day 210 CHMP discussion and decision on need for adoption of a LoOI and/or an oral explanation

4. ATMP EVALUATION

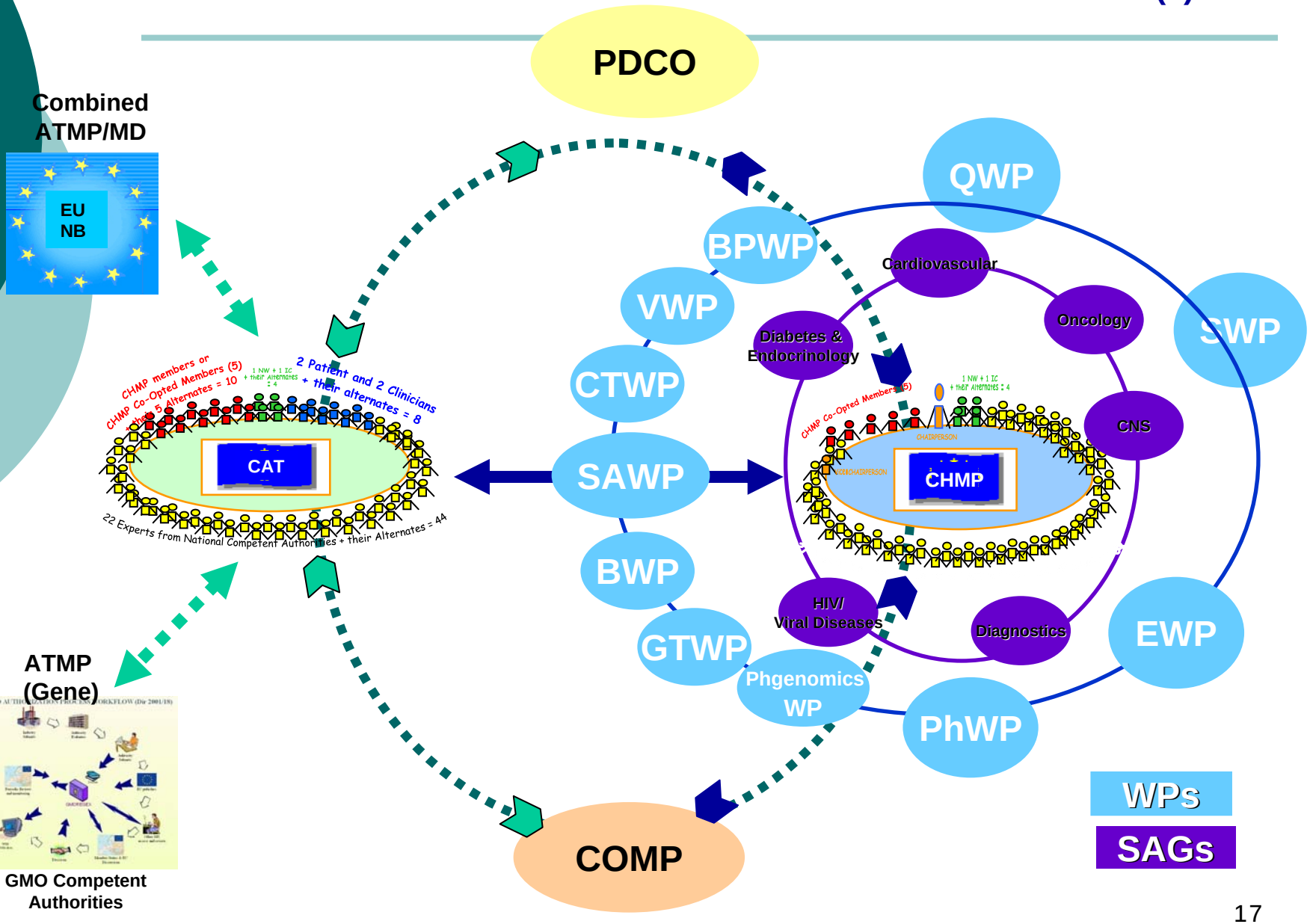
SPECIFIC RULES FOR THE EVALUATION OF COMBINED PRODUCTS

Product as a whole is **subject to evaluation by the CAT**

- the Agency **must recognise the results** of any assessment by a **notified body** in accordance with Directives 93/42/EEC or 90/385/EEC of the medical device part or active implantable medical device part (but may request the relevant notified body to transmit any information related to its assessment)
- if the application does not include the results of the assessment by a notified body, it **shall seek an opinion from a notified body**, **unless the CAT advised by its experts for medical devices decides that involvement of a notified body is not required**

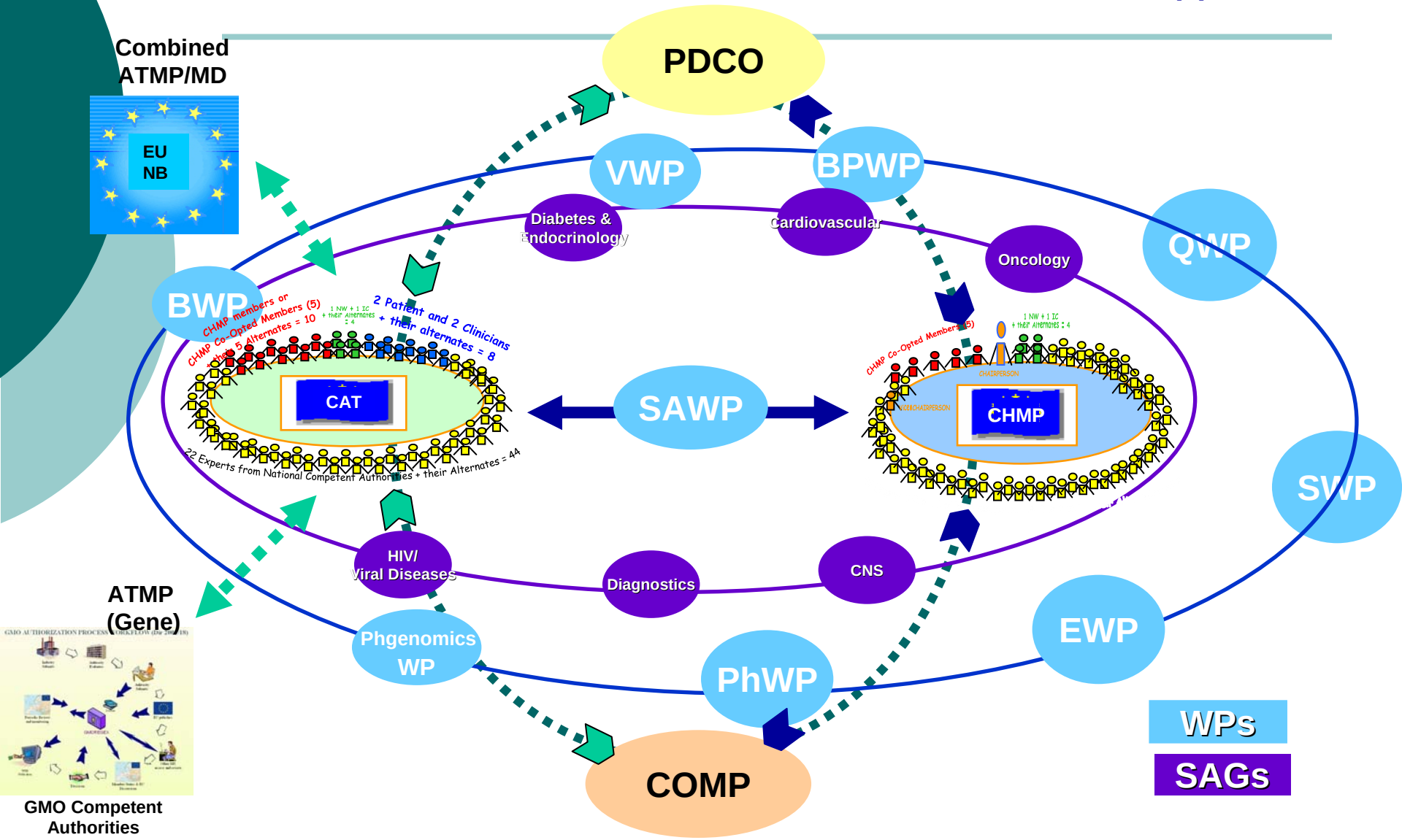
4. ATMP EVALUATION

OTHER/NEW INTERACTIONS NEEDED FOR ATMPs EVALUATION (1)



4. ATMP EVALUATION

OTHER/NEW INTERACTIONS NEEDED FOR ATMPs EVALUATION (2)

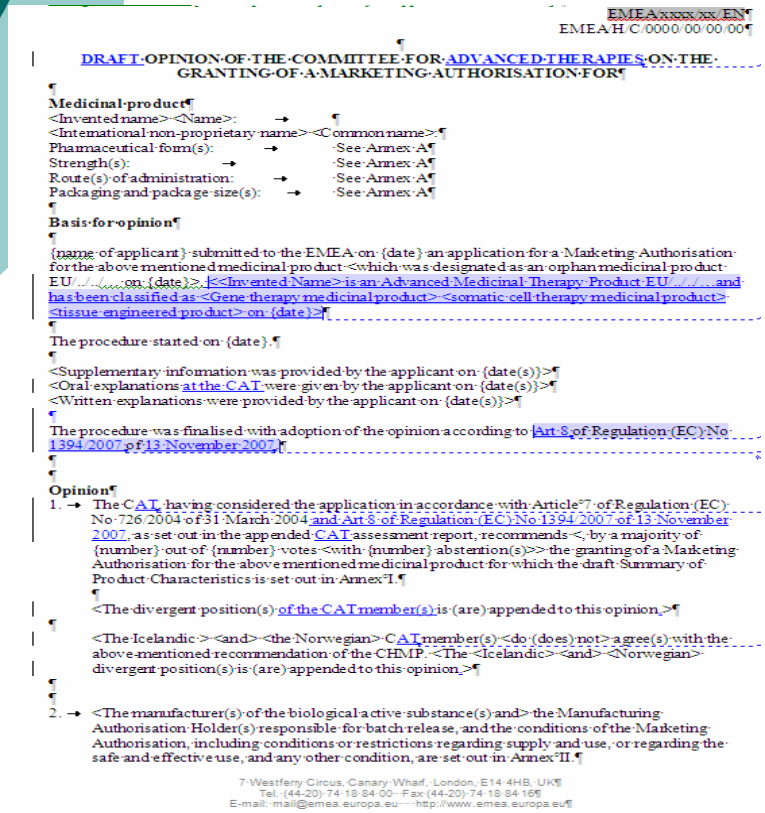


4. ATMP EVALUATION

Draft opinion prepared by CAT for final adoption by CHMP

Draft Opinion adopted by CAT

CHMP Opinion



EMEA/xxxx/xx/EN
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DRAFT OPINION OF THE COMMITTEE FOR ADVANCED THERAPIES ON THE GRANTING OF A MARKETING AUTHORISATION FOR

Medicinal product

<Invented name>: <Name>: → See Annex A
<International non-proprietary name>: <Common name>:
Pharmaceutical form(s): → See Annex A
Strength(s): → See Annex A
Route(s) of administration: → See Annex A
Packaging and package size(s): → See Annex A

Basis for opinion

{name of applicant} submitted to the EMEA on {date} an application for a Marketing Authorisation for the above mentioned medicinal product <which was designated as an orphan medicinal product EU/../../.. on {date}>, [<<Invented Name> is an Advanced Medicinal Therapy Product EU/../../.. and has been classified as <Gene therapy medicinal product> <somatic cell therapy medicinal product> <tissue engineered product> on {date}>]

The procedure started on {date}.

<Supplementary information was provided by the applicant on {date(s)}>
<Oral explanations at the CAT were given by the applicant on {date(s)}>
<Written explanations were provided by the applicant on {date(s)}>

The procedure was finalised with adoption of the opinion according to Art 8 of Regulation (EC) No 1394/2007 of 13 November 2007.

Opinion

1. → The CAT, having considered the application in accordance with Article 7 of Regulation (EC) No 726/2004 of 31 March 2004 and Art 8 of Regulation (EC) No 1394/2007 of 13 November 2007, as set out in the appended CAT assessment report, recommends <, by a majority of {number} out of {number} votes <with {number} abstention(s)>> the granting of a Marketing Authorisation for the above mentioned medicinal product for which the draft Summary of Product Characteristics is set out in Annex I.

<The divergent position(s) of the CAT member(s) is (are) appended to this opinion.>

<The Icelandic > <and> <the Norwegian> CAT member(s) <do (does) not> agree(s) with the above-mentioned recommendation of the CHMP. <The <Icelandic> <and> <Norwegian> divergent position(s) is (are) appended to this opinion.>

2. → <The manufacturer(s) of the biological active substance(s) and> the Manufacturing Authorisation Holder(s) responsible for batch release, and the conditions of the Marketing Authorisation, including conditions or restrictions regarding supply and use, or regarding the safe and effective use, and any other condition, are set out in Annex II.

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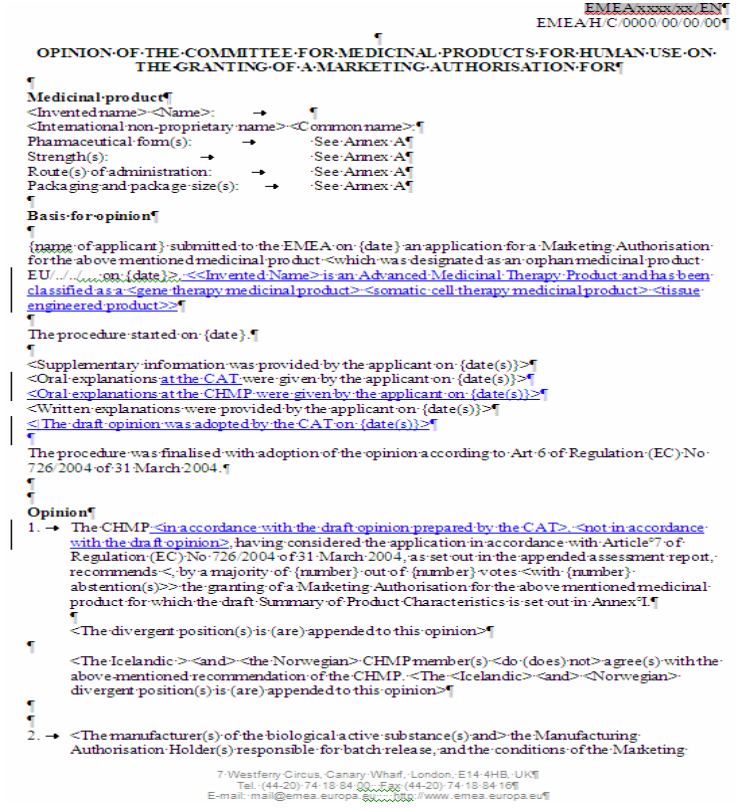

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OPINION OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE ON THE GRANTING OF A MARKETING AUTHORISATION FOR

Medicinal product

<Invented name>: <Name>: → See Annex A
<International non-proprietary name>: <Common name>:
Pharmaceutical form(s): → See Annex A
Strength(s): → See Annex A
Route(s) of administration: → See Annex A
Packaging and package size(s): → See Annex A

Basis for opinion

{name of applicant} submitted to the EMEA on {date} an application for a Marketing Authorisation for the above mentioned medicinal product <which was designated as an orphan medicinal product EU/../../.. on {date}>, <<Invented Name> is an Advanced Medicinal Therapy Product and has been classified as a: <gene therapy medicinal product> <somatic cell therapy medicinal product> <tissue engineered product>>

The procedure started on {date}.

<Supplementary information was provided by the applicant on {date(s)}>
<Oral explanations at the CAT were given by the applicant on {date(s)}>
<Oral explanations at the CHMP were given by the applicant on {date(s)}>
<Written explanations were provided by the applicant on {date(s)}>
<The draft opinion was adopted by the CAT on {date(s)}>

The procedure was finalised with adoption of the opinion according to Art 6 of Regulation (EC) No 726/2004 of 31 March 2004.

Opinion

1. → The CHMP <in accordance with the draft opinion prepared by the CAT>, <not in accordance with the draft opinion>, having considered the application in accordance with Article 7 of Regulation (EC) No 726/2004 of 31 March 2004, as set out in the appended assessment report, recommends <, by a majority of {number} out of {number} votes <with {number} abstention(s)>> the granting of a Marketing Authorisation for the above mentioned medicinal product for which the draft Summary of Product Characteristics is set out in Annex I.

<The divergent position(s) is (are) appended to this opinion>

<The Icelandic > <and> <the Norwegian> CHMP member(s) <do (does) not> agree(s) with the above-mentioned recommendation of the CHMP. <The <Icelandic> <and> <Norwegian> divergent position(s) is (are) appended to this opinion>

2. → <The manufacturer(s) of the biological active substance(s) and> the Manufacturing Authorisation Holder(s) responsible for batch release, and the conditions of the Marketing

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4. ATMP EVALUATION

New QRD templates (draft)

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

[NOTE: the following are those items of information required by Article 11 of Directive 2001/83/EC, as amended, and current practice in the centralised procedure. In the case of advanced therapy medicinal products, these items are listed in Annex II of Regulation (EC) 1394/2007.
This guidance should be read in conjunction with the relevant guidelines that can be found on the EMEA website (See also "Convention" for format and layout):
http://www.emea.europa.eu/htms/human/qrd/docs/convention.pdf, in particular the "Guideline on Summary of Product Characteristics" as published on the Website of the European Commission in the Notice to Applicants, Volume 2C: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol2_en.htm

During the evaluation process, applicants may present SPCs for different strengths in one document, clearly indicating with grey-shaded titles the strength or presentation to which alternative text elements refer. However, a separate SPC per strength and per pharmaceutical form, containing all pack-sizes related to the strength and pharmaceutical form concerned will have to be provided by the applicant as follows:

- *English language version: immediately after adoption of the opinion*
- *All other language versions: at the latest 22 days after adoption of the opinion (i.e. at the latest after incorporation of Member States comments).*

See also: The new Product Information linguistic review process for new applications in the Centralised Procedure - http://www.emea.europa.eu/pdfs/human/regaffair/554202en.pdf

Standard statements are given in the template, which must be used whenever they are applicable. If the applicant needs to deviate from these statements to accommodate product-specific requirements, alternative or additional statements will be considered on a case-by-case basis.

Bracketing convention:
{text}: Information to be filled in
<text>: Text to be selected or deleted as appropriate]

5. RE-EXAMINATION PROCEDURE (1)

- Legal timeframes of 15 days and 60 days (calendar days) re-examination evaluation **WITHOUT** Clock stops
- Same concept of CAT/CHMP Assessment Teams BUT new Assessment Team to be re-appointed
- CAT must be consulted by CHMP in re-examination [Art. 8 of Regulation (EC) No 1394/2007]
- CAT must provide CHMP with a "Draft opinion of re-examination" [Art. 8 of Regulation (EC) No 1394/2007]
- Oral explanations may have to be scheduled in limited timeframe in front of (SAG), CAT and/or CHMP

5. RE-EXAMINATION PROCEDURE (2)

- Same evaluation process as initial evaluation
- Systematic SAG consultation if requested by the applicant/MAH,
- If not requested, as per normal procedure CAT/CHMP may request it
- Transparency: Draft opinion adopted by CAT to be reflected in SMOPs/CHMP Press Releases/CHMP Monthly report publications.

6. WITHDRAWAL

The **withdrawal process** will not change for ATMPs **but** can happen **before or after draft opinion** adopted by CAT ! (same principles of confidentiality apply)

- The applicant shall communicate the reasons to withdraw the application
- The EMEA shall make this **information publicly accessible** and shall publish the assessment report, if available, after deletion of all information of a commercially confidential nature (as justified by the applicant). Withdrawal of the application after adoption of the opinion does not prevent that this information is made publicly available.

7. POST-AUTHORISATION

- Post-authorisation procedures will follow the same principles as for the initial evaluation
- Variation Regulation 1234/2008 will be implemented (end 2009)
- Procedural advice on evaluation of ATMPs will be updated to add the post-authorisation procedures

8. 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

8. 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

Draft opinion prepared by the CAT will be reflected in the CHMP press release

Thank you for your attention

European Medicines Agency

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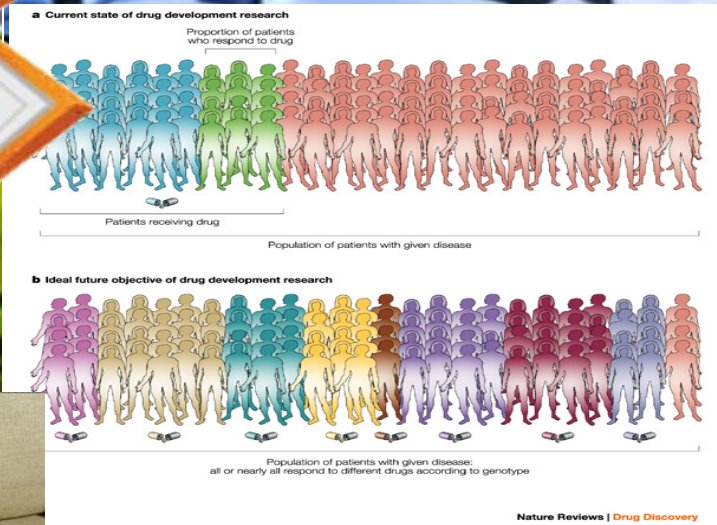
ANY QUESTION ?



INTRODUCTION

ATMP DRUG DEVELOPMENT