Marketing Authorisation: The Evaluation Process

Dr Evdokia Korakianiti
Scientific Administrator
Centralised Procedure

It is one of a number of ‘procedures’ or ‘routes’ to authorisation in the EU

It is a regulatory assessment process leading to:

- 1 Marketing Authorisation (simultaneously valid in ALL EU MS)
- 1 Invented Name
- Identical product information, in all 23 EU languages:
  - Summary of Product Characteristics (SPC) which defines the conditions of use of the product – indications, warnings, shelf-life, etc.
  - Package Leaflet (Information for the patient)
  - Package Labelling (Information on the carton)
- Maximum time limit
  - 210 days Evaluation ➔ Opinion
• The centralised evaluation system is designed to coordinate the existing scientific resources of Member States.

• EMEA is coordinating the scientific evaluation → Scientific Opinion

• The European Commission grants the Commission Decision (Pan European Marketing Authorisation) on the basis of this Opinion.

• Legally binding to all MS.
Partners in the Centralised Procedure

- **European Commission (Pharmaceutical Committee)**
  - Converts the CHMP opinion into a Decision – i.e. an authorisation

- **Applicant**

- **CHMP**
  - Committee on Human Medicinal Products
  - Final opinion on all product-related scientific disputes

- **EMEA secretariat**
  - Coordinates activities and facilitates the CHMP opinion (whether positive or negative!)

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**EMEA**
The applicant has to submit a ‘dossier’ of scientific information on quality, efficacy and safety to support the application.

The CHMP appoints two of its members to act as “Rapporteurs” who will do the evaluation on behalf of the Community.

Each Rapporteur has a team of experts in the field of Quality, Safety, Efficacy, so two teams will evaluate the dossier.

The Rapporteurs’ assessment is a recommendation to CHMP and forms the basis of the discussion.

Transparent procedure, the Rapporteurs’ assessment is sent to the applicant.
• The decision on whether to recommend the granting of an authorisation is taken by **All** CHMP members

• CHMP Opinions are based on majority, **if a MS does not agree it will still have to comply with the majority view**

• For “unusual” cases the CHMP may seek the advise of specialised experts (Working Parties, SAGs)
The main scientific principle used in the evaluation of medicines is the benefit/risk ratio based on quality, efficacy, safety and risk management considerations.
Centralised Procedure - Overview

- Pre-submission
- Submission-Validation
- Primary Evaluation
- Secondary Evaluation
- Stop Clock
- Opinion/Decision
- Post Authorisation

**Day 0**
- D.120
- 'first phase'

**Day 1**
- D.121
- 'second phase'

**Post Authorisation**
- D.210
- D.277

Legal requirement !: CHMP Opinion within **210** days
Submission:  
- Applicant submits the dossier.  
- Dossier requirements are defined in the legislation and in relevant guidelines

Validation:  
- Performed by the EMEA  
- 10 working days from submission date  
- No scientific evaluation, at this point  
- Only check of:  
  - the completeness of the dossier and  
  - compliance with legal/regulatory requirements
Primary Evaluation Phase

- **D 80** → Rapp./Co-Rapp initial Assessment Report to CHMP → also sent to applicant - first response from the system
- **D 100** → CHMP comments
- **D 120** → Formal CHMP Overview, provisional Recommendation, and consolidated List of Questions (LoQ)

Pre-submission → Submission-Validation → Primary Evaluation → Stop Clock → Secondary Evaluation → Opinion Decision → Post Authorisation
Applicant’s responses expected within **3 months**
May be extended up to 6 months
Optional clarification meeting on LoQ (Applicant / Rapporteurs)
Secondary Evaluation Phase

Day 0
Submission-Validation

Day 1
Primary Evaluation

D 120
Stop Clock

D 121
Secondary Evaluation

D 210
Opinion

D 277
Decision

Stop
Clock

D 150 → Joint Rapp./Co-Rapp AR
D 170 → CHMP comments

D 180 → Outstanding issues?

Yes

No

Day 181
Hearing

D 210
Opinion

D 180
Opinion

Need for a hearing?

Stop Clock
Types of Opinion

- **Positive**
- **Negative**
- **Under Exceptional Circumstances**
  - Comprehensive data cannot be provided
  - Reviewed annually to reassess the risk-benefit balance
- **Conditional**
  - Additional data is required, however the benefit to public health of immediate availability outweighs risk
  - Authorisation valid for one year, on a renewable basis
  - Once the pending studies are provided, it can become a “normal” marketing authorisation
CHMP Opinion

- **Annex A**: pack sizes, pharmaceutical forms, etc
- **Annex II**: manufacturers, legal status, etc
- **Annex IV**: conditions to be implemented by the MS

- **Appendix to the Opinion**:  
  - CHMP Assessment Report (summary of the scientific evaluation)

Single harmonised SPC, Labelling and Package Leaflet
The applicant can appeal against the CHMP Opinion

- 15 days to appeal
- 60 days to submit grounds for appeal
- CHMP 60 days to consider revision of initial opinion
  - No new data
  - Scientific advisory group may be consulted
**Post Opinion phase Timelines**

- **Product information v.1 (MAH) + Annex A + Form 1**
- **Member State Review (QRD/CxMP)**
- **Product information v.2 (MAH) + Form 2**
- **PIQ final check (implemented comments)**
- **Product information v.3 (EMEA)**

**Day Timelines**

- Day 210: Opinion
- Day 215: Comments from MS + Form 1
- Day 229: Transmission to Commission
- Day 232: Commission: Start Standing Committee consultation
- Day 237: Translation check of product information
- Day 239: End Standing Committee consultation
- Day 261: Final Commission Decision
- Total time: 67 days

**Performing Entity**
- **EC Decision Making Process**
- **Translation check of product information**
- **Performed by the EMEA for SMEs**
Transparency

- CHMP Monthly report
- CHMP Press release
- European Public Assessment Report (EPAR)
  - It is published in modular form on the EMEA website. Contains:
  - The summary of the scientific evaluation of a product in EN
  - Product Information is published in all EU languages.

(http://www.emea.europa.eu/index/indexh1.htm)
Accelerated procedure

- CHMP opinion in 150 days (instead of 210)
- 1st phase similar
- Day 120 Opinion or List of outstanding issues
- Day 121-150 Oral explanation if applicable + Opinion
Products do not stand still, they are changing all the time.

Any change to the approved Marketing Authorisation requires regulatory approval.

There are different procedures for post authorisation changes depending on the nature of the proposed change (minor / major).
Closing Remarks

The Centralised Procedure:

• 1 application, 1 evaluation, 1 authorisation
• EU-wide authorisation binding and identical in all MS
• Provides access at the same time to potentially nearly half a billion patients
• Set timelines → Scientific Opinion in 210 days, followed by authorisation ~ 2 months later
• Transparent procedure, reports are released to applicants and EPARs are published on the EMEA website.
• Support to SMEs
  – Scientific advice from CHMP: reduced fee
  – Procedural assistance from EMEA Secretariat
  – Translations of product information performed by EMEA (no fee)
THANK YOU!

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