The EU system for marketing authorition

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The EU system for Marketing Authorization

❑ Key Principles of EU Pharmaceutical Law & Policy

Objectives

Protection of public health

Free movement of medicinal products within the EU

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❑ Key Milestones

1965

First EU legislation on medicinal products.

- To prevent a recurrence of the **thalidomide** disaster
- To safeguard public health by not allowing medicinal products ever again to be marketed without **prior authorisation**
- Authorization only granted after demonstration of the: **safety**, efficacy and **quality** of the product

1995

Establishment of:

- The EU **centralized authorization** system for medicinal products
- The **European Medicines Agency** (EMA)

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❑ Key Actors

LEGISLATION

Proposal:

European Commission

Adoption:

European Council

+

European Parliament

Implementing Acts:

European Commission

+

Committee of EU MSs

Interpretation:

European Court of Justice

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❑ Key Actors

AUTHORIZATIONS

Centralised Procedure

Application to:

European Medicines Agency EMA

→

Decision:

European Commission

+

Committee of EU MSs

Appeal:

European Court of Justice

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❑ Marketing Authorizations

A medicinal product may only be placed on the market in the European Union when a **marketing authorisation** has been issued:

- by the **competent authority of a Member State** (National authorisations) or
- by the **Commission** for the **whole EU** (Union authorisation).

Authorisations are granted on the basis of the criteria of QUALITY, SAFETY and EFFICACY

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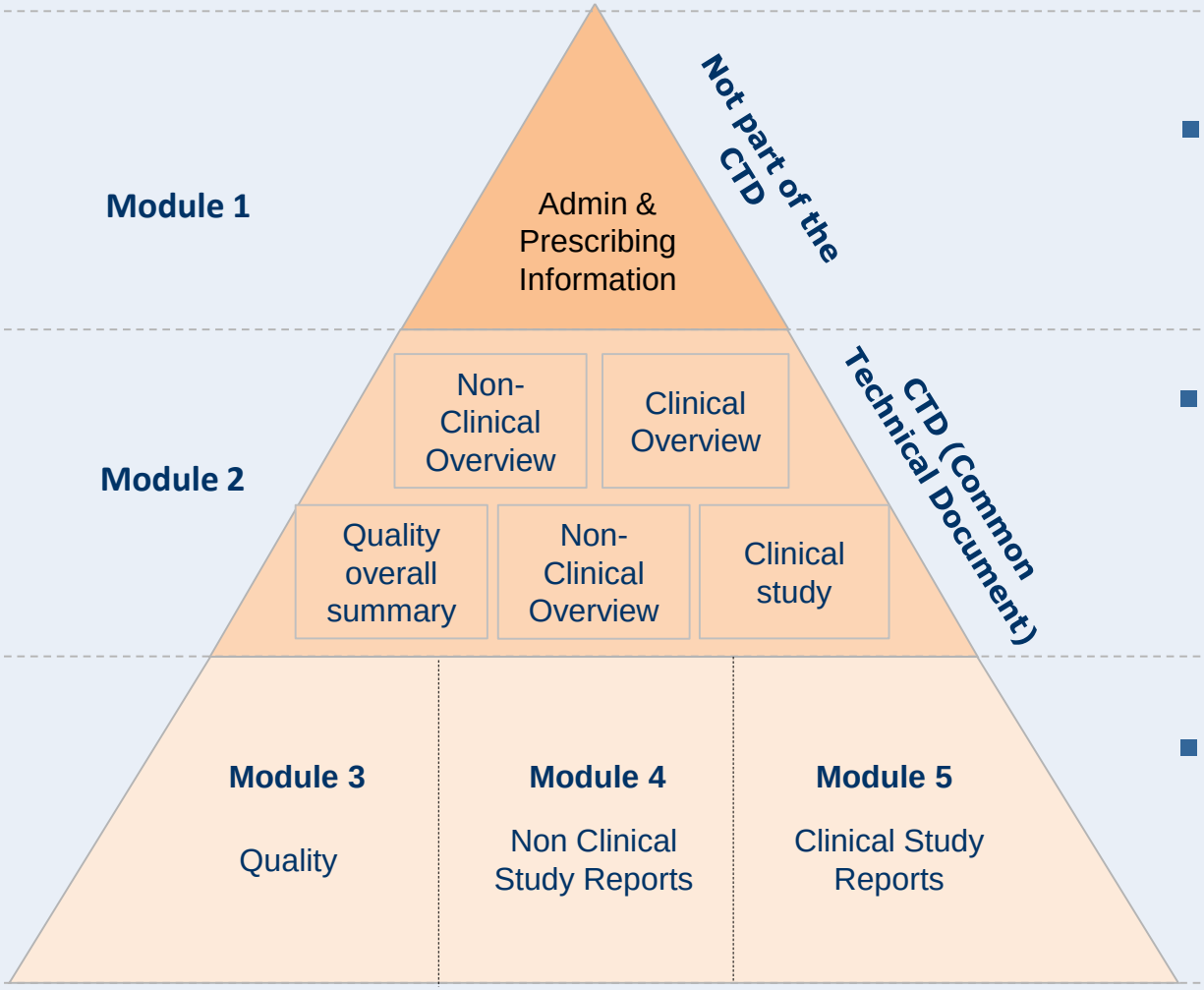
❑ Application requirements



- Authorisation of medicines in the EU reflects the internationally agreed standards
- EU–CTD (Common Technical Document) presentation is applicable irrespective of the type of procedure (centralised, mutual recognition or national).
- Companies need to submit data of tests and trials, demonstrating the Efficacy, Safety and Quality of the medicinal product.

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❑ The procedural set-up

Approval in one Member State	➢ National Authorisation
Approval in several or all Member States	➢ Mutual Recognition Procedure (MRP) ➢ Decentralised Procedure (DCP) ➢ Centralised Procedure (CP)

ROUTE? CHOICE?

Depends on:

- Type of product
- Authorisation history in EU
- Regulatory & marketing strategy
- Company preferences etc …

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❑ Procedures for granting a marketing Authorization

Mutual Recognition Procedure (MRP)	Decentralised Procedure (DCP)	Centralised Procedure (CP)

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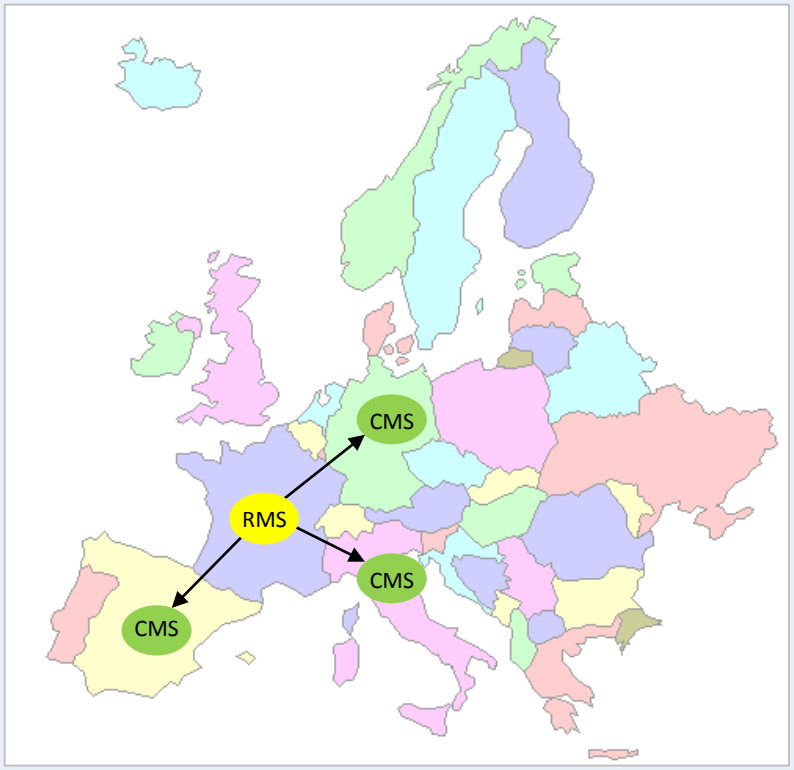
❑ Mutual Recognition Procedure

Mutual Recognition Procedure (MRP)	Decentralised Procedure (DCP)	Centralised Procedure (CP)



- Starts from an **already existing national marketing authorisation** granted by one Member State – the **Reference Member State (RMS)**
- One or more Member States – the **Concerned Member States (CMS) –** are asked to **recognize** the authorization granted by the Reference Member State.
- In case of disagreement the matter is referred to:
- - the **CMDh** (60 days), and, if needed, to
- - the **CMPH** (60 days).

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❑ Mutual Recognition Procedure (MRP)

Authorisation in one Member State, the Reference Member State **(RMS)** (210 days)

Submission to chosen Concerned Member States **(CMS)** for recognition of Authorisation (90 days)

Authorisation in **CMS** (within 30 days)

In case of disagreement referral to **CMD(h)/CHMP** (60 + 60 days)

Serious risk to public health

Referral to **CMD(h)**

CMD(h) : Coordination Group for Mutual Recognition and Decentralised Procedures – Human

CHMP : Committee for Medicinal Products for Human Use **(EMA)**

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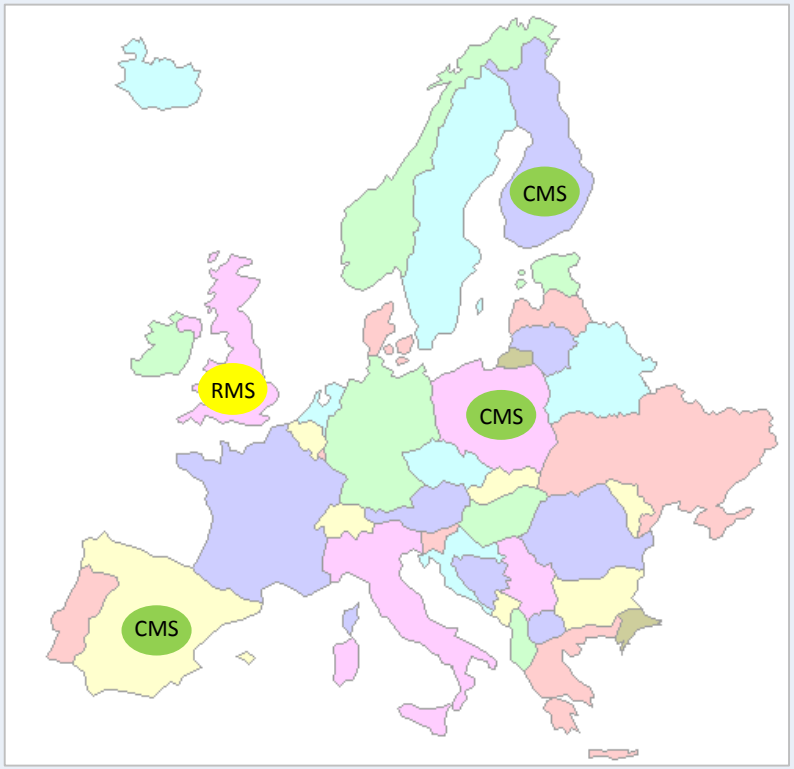
❑ Decentralised Procedure

Mutual Recognition Procedure (MRP)	**Decentralised Procedure (DCP)**	Centralised Procedure (CP)



- No pre-existing **marketing authorisation** granted by one Member State.

- Simultaneous application to a **RMS** and several **CMS**.
- Assessment by **RMS** and reactions by the **CMS.**

- In case of disagreement the matter is referred to:
- - the **CMDh** (60 days), and, if needed, to
- - the **CMPH** (60 days).

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❑ Decentralised Procedure (DCP)

- No MA existing in EEA
- Application to **RMS** & **CMS**
- Initial assessment by **RMS** and comments by **CMS** (120 days)

Second phase of assessment and position by Member States (90 days)

Authorisation in **CMS** (within 30 days)

In case of disagreement referral to **CMD(h)/CHMP** (60+ 60 days)

CMD(h) : Coordination Group for Mutual Recognition and Decentralised Procedures – Human

CHMP : Committee for Medicinal Products for Human Use **(EMA)**

Serious risk to public health

Referral to **CMD(h)**

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Mutual Recognition Procedure (MRP)	Decentralised Procedure (DCP)	Centralised Procedure (CP)

- Single application to place the product on the market throughout the European Union.

- Scientific assessment made by the **EMA**.
- Authorisation granted by **the European Commission**, after consulting a committee of **Member States**

- Marketing authorisation, **valid in all Member States**
- **Product name** identical in all Member States
- Authorization **managed** by EMA/Commission

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❑ Centralised Procedure (CP)

Mandatory

Biotech, AIDS, Diabetes, Cancer, Orphan, Neurodegenerative

Optional

Significant therapeutic, scientific or technical innovation

Application dossier sent to EMA

EMA validation (14 days) → **Checks application meets criteria**

CHMP starts evaluation (Day 0) → **Clock starts - Reviews by rapporteur and corapporteur**

List of questions sent to applicant (Day 120) → **Review clock stops (up to 3 months)**

Potential for further questions and clock stops for responses or oral explanation

Responses submitted by applicant (Day 121) → **Review clock restarts**

CHMP Opinion (Day 210) → **Review ends**

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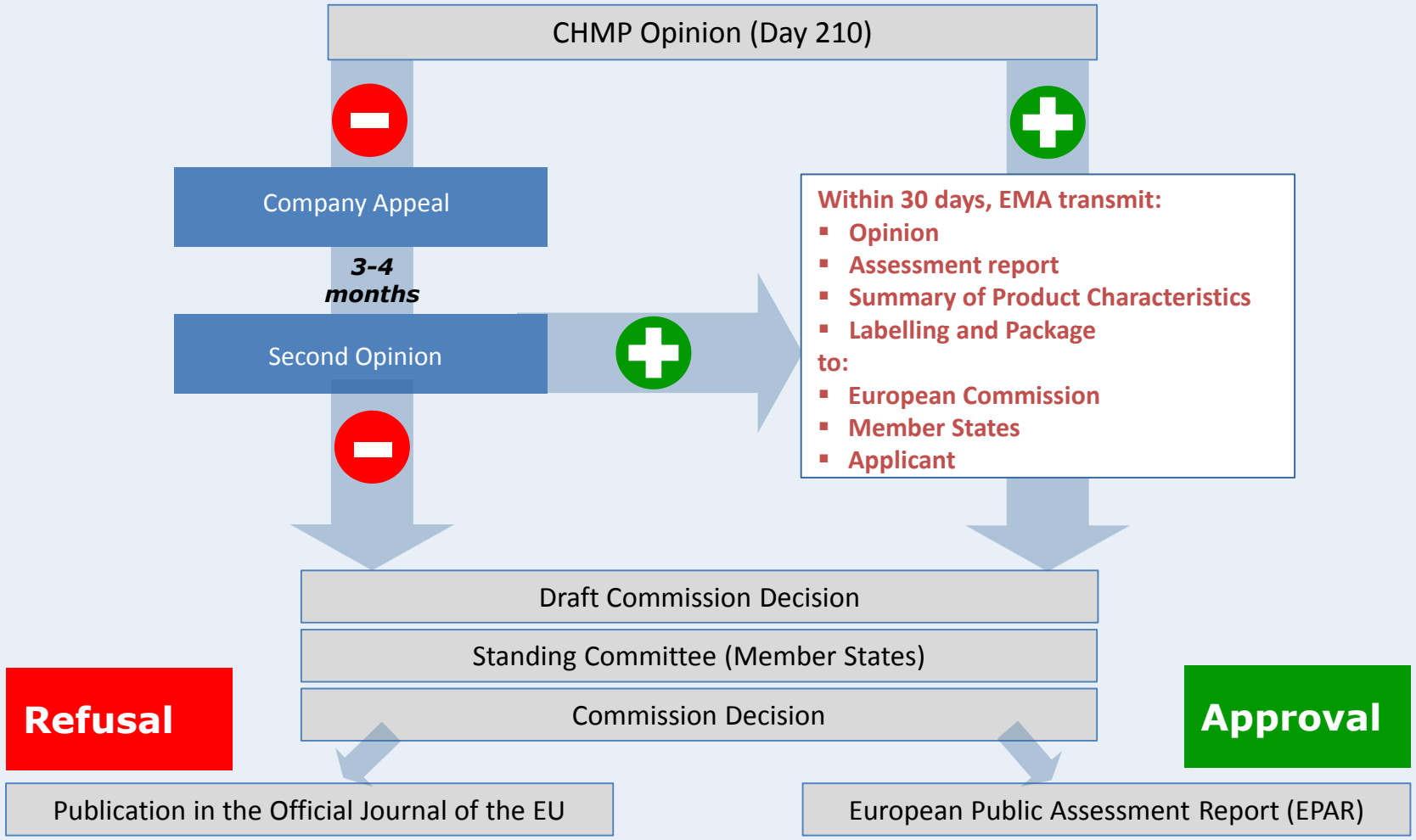
❑ Centralised Procedure (CP)



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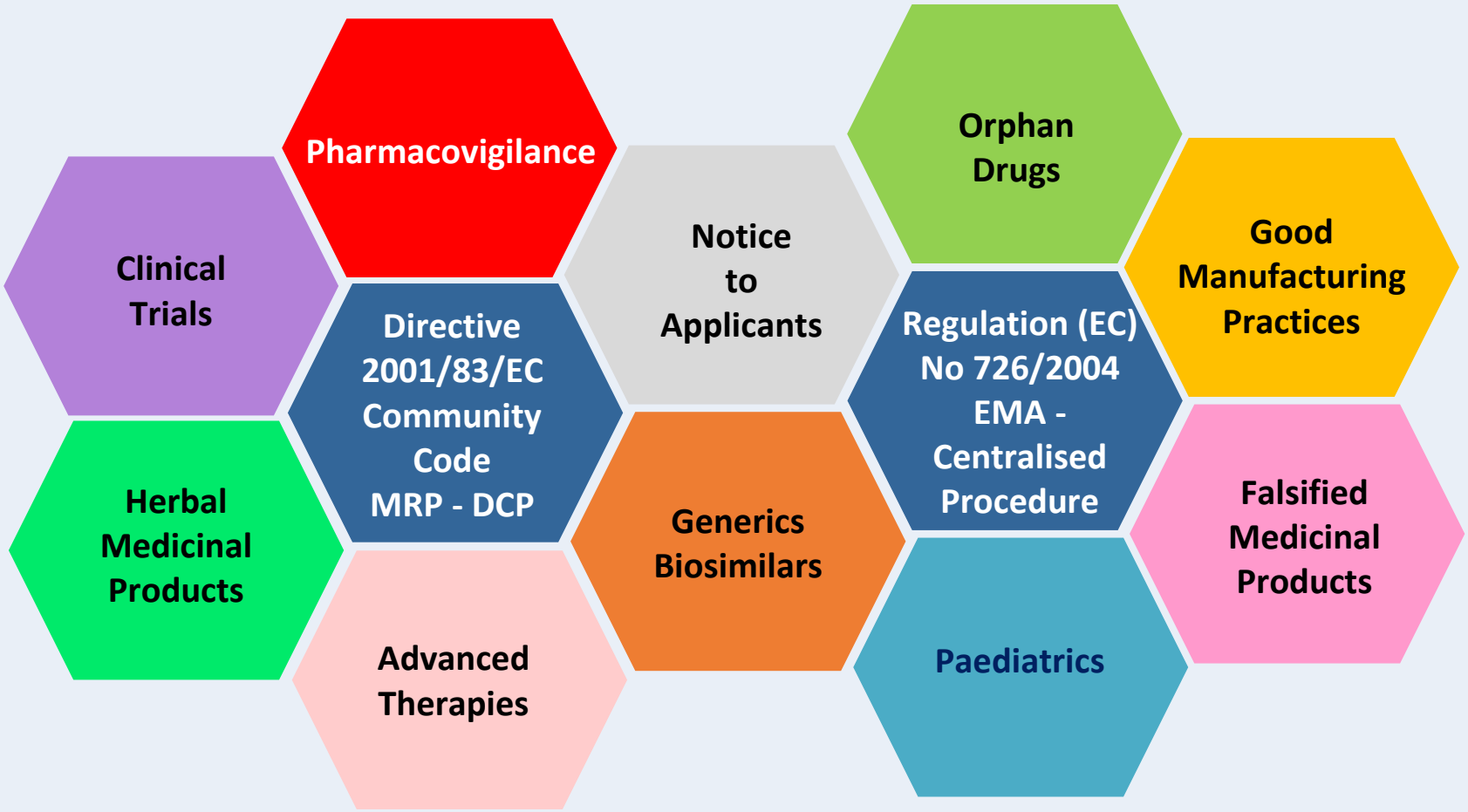
❑ EU Pharma Legislation



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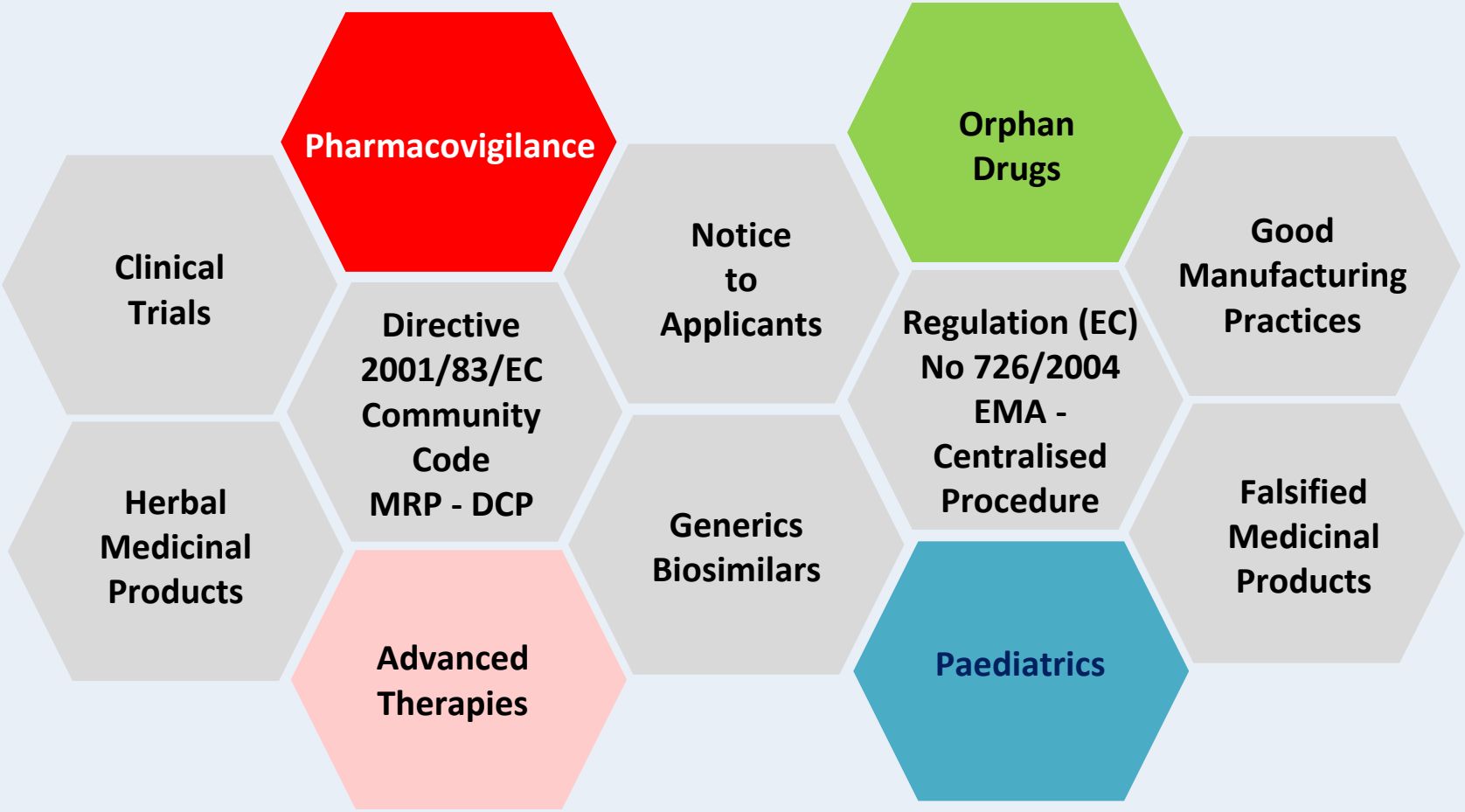

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Pharmacovigilance

Principles

Pharmacovigilance is the process and science of monitoring the safety of medicines and taking action to reduce the risks and increase the benefits of medicines.

Related activities	• **Collecting and managing data** on the safety of medicines (RMP, PSURs) • Evaluating the data to **detect 'signals'** (any new or changing safety issue) • Acting to **protect public health** (incl. regulatory action) • **Communicating** with/informing stakeholders and public
Stakeholders	• **Users of medicines (reporting ADRs)** • **Health care professionals** working with medicines • **Regulatory authorities**, including the European Medicines Agency(EMA) and those in the Member States in charge of the safety of medicines • Pharmaceutical **companies** and companies importing or distributing medicines

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Pharmacovigilance

Functionning

TRIGGERS OF THE DECISION MAKING PROCEDURE

- Monitoring ADRs
- Signal of a new AE, ADR
- Periodic safety update reports
- Oversight of post-authorisation obligations
- Specific procedure: referrals

ACTIONS BASED ON PHV CONCERNS

- Change of MA
- Suspension
- Withdrawal
- Revocation
- Non-renewal

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Pharmacovigilance

Withdrawal of marketing authorization

The competent authorities suspend, revoke or vary an authorization if:

- the product proves to be harmful in the normal conditions of use,
- its therapeutic efficacy is lacking,
- risk-benefit balance is not favourable,
- its qualitative and quantitative composition is not as declared
- certain conditions related to MA not fulfilled.

Products are withdrawn from the market, if:

- the above listed reasons are present,
- the controls on the medicinal product and/or on the ingredients and the controls at an intermediate stage of manufacturing have not been carried out,
- other requirements or obligations relating to the granting of the manufacturing authorisation has not been fulfilled.

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Orphan Drugs

Regulation (EC) No 141/2000

Criteria for designation:

- Rare disease (not more than 5 in 10,000 persons in the EU) or not sufficient return on investment
- Seriousness: life-threatening or chronically debilitating
- No satisfactory method of treatment or if existing significant benefit has to be demonstrated

Incentives:

- 10 years of market exclusivity
- Protocol assistance (fee reduction for product development)
- EU marketing autorisation
- Eligible for national incentives

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Orphan Drugs

Regulation (EC) No 141/2000

Some figures:

- 1340 products in development designated as orphan medicinal products by the European Commission
- 125 orphan medicinal medicines authorised by the European Commission (one on the basis of the 'insufficient return on investment' criterion)
- 84% of new active substance

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Paediatrics

Regulation (EC) 1901/2006

Facts:

- 21% of Europeans are **children**
- **Children** are not just small adults
- Situation prior to the paediatric legislation:
  - Absence of age- and development-related research and lack of suitable products
  - Recurrent off-label use
  - Economic/ethical factors
  - Experience prevails evidence

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Paediatrics

Basic features

Aim	▪ Ensure high-quality research into developments of medicines for children ▪ Ensure that over time majority of medicines used for children are authorised for such use ▪ Ensure availability of high-quality information about medicines used by children
Scope	▪ New products ▪ Line extensions of a patent-protected product ▪ PUMA (Paediatric Use Marketing Authorisation)
Procedure	▪ Paediatric Investigation plan ▪ Waiver/Deferral ▪ Authorisation
Actors	▪ Industry/Paediatric Committee at EMA/National Competent authorities
Rewards/ Incentives	▪ 6 month SPC prolongation ▪ 2 year extension market exclusivity for orphan medicinal products ▪ Scientific advice/protocol assistance/EU-funded research

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Paediatrics

International comparison

	U.S. BPCA	U.S. PREA	EU
Development	Optional	Mandatory	Mandatory (off-patent optional)
Instrument	Written Request (PPSR)	PSP	PIP
Waiver	--	criteria for full and partial waivers	criteria for full and partial waivers
Submission Timing	Anytime adequate data available	End of Phase 2 (EOP2)	End of Phase 1 (EOP1)
Reward	6 months patent extension	--	6 months patent extension
Drugs & Biologics	Yes	Yes	Yes
Orphan	Included	Excluded	Included

Canada: 6 month extension data protection / Switzerland: EU system

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Advanced Therapies

Regulation (EC) 1394/2007

Background

- Advanced therapy medicinal products are new medical products based on **genes** (gene therapy), **cells** (cell therapy) and **tissues** (tissue engineering).
- These advanced therapies herald revolutionary treatments of a number of diseases or injuries, such as skin in burns victims, Alzheimer's, cancer or muscular dystrophy. They have huge potential for patients and industry.
- The lack of an EU-wide regulatory framework hindered patients' access to products, hampered the growth of this emerging industry and ultimately affected EU competitiveness in a key biotechnology area.
- The EU rules are designed:
  - to ensure the free movement of advanced therapy products within Europe,
  - to facilitate access to the EU market and
  - to foster the competitiveness of European companies in the field, while guaranteeing the highest level of health protection for patients.

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Advanced Therapies

Regulation (EC) 1394/2007

Regulation (EC) 1394/2007

- A **centralised** marketing authorisation procedure, to benefit from the pooling of expertise at European level and direct access to the EU market.
- A new and multidisciplinary expert Committee (**Committee for Advanced Therapies**), within the European Medicines Agency (EMA), to assess advanced therapy products and follow scientific developments in the field.
- Technical requirements **adapted to the particular characteristics** of these products.
- Special **incentives for small and medium-sized enterprises**.
- This Regulation also marks the recognition that a number of advanced therapy products actually combine biological materials, such as tissues or cells, and chemical structures such as metal implants or polymer scaffolds. These **combination products** lie at the border of the traditional pharmaceutical area and other fields (e.g. medical devices).

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Thank You !