Diploma e Master Universitario in Alti Studi Europei
Collegio Europeo di Parma

Seminar on: "EU Pharmaceutical Policy" 2018

MORNING **Monday 9 April 2018**

Location: Collegio Europeo di Parma, Via Università 12, Parma

09:00 - 10:30	***EU Pharmaceutical Law and Policy*** Prof. Patrick Deboyser
10:30 - 11:00	*Coffee break*
11:00 - 12:30	***Pharmaceutical Markets and Economy*** Ms Nathalie Moll, Director General of the European Federation of Pharmaceutical Industries and Associations (EFPIA)

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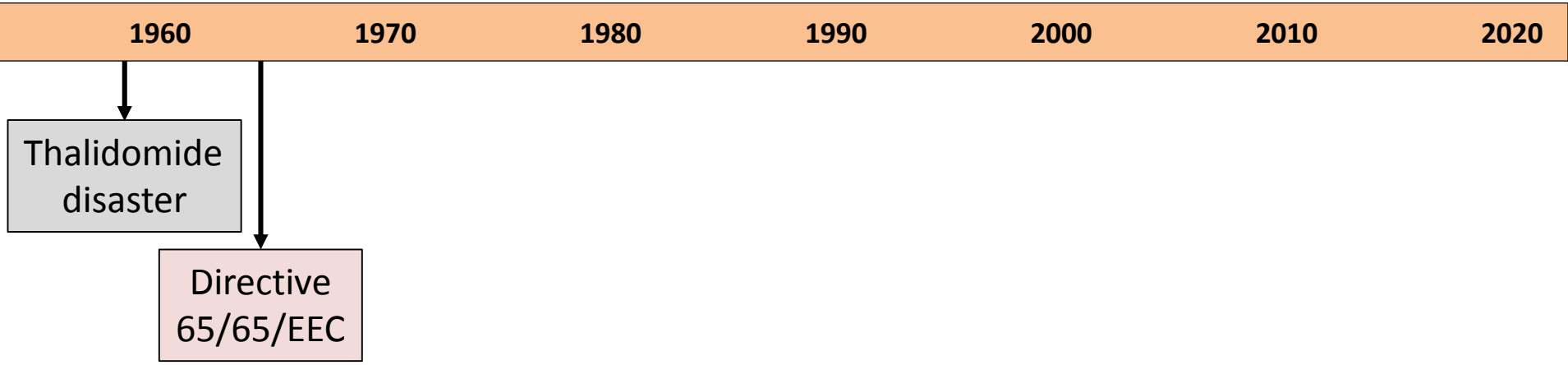
AFTERNOON **Monday 9 April 2018**

Location: Chiesi Farmaceutici S.p.A., Via Palermo 26/A, Parma	
14:30 - 15:00	***Outlines of pharmaceutical discovery and development*** Dr Andrea Chiesi, CEO - Holostem, R&D Portfolio Manager - Chiesi Group
15:00 - 15:30	*Coffee break*
15:30 - 16:00	**Visit of Chiesi Farmaceutici Research Centre**

1960 | 1970 | 1980 | 1990 | 2000 | 2010 | 2020

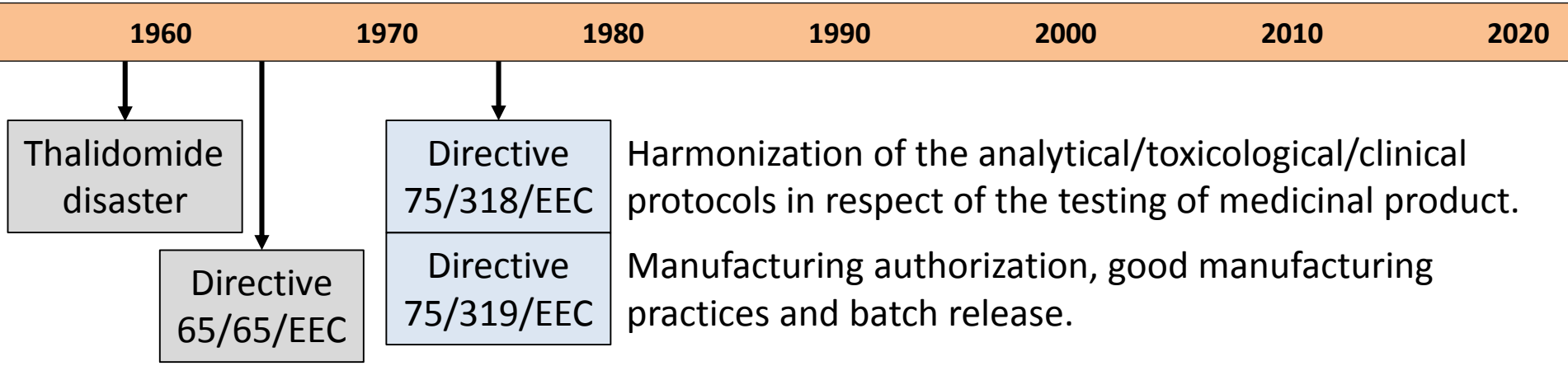
Thalidomide disaster

- New sedative/hypnotic first marketed in Germany in 1957 to treat:
  - anxiety, insomnia, gastritis, and hypertension,
  - morning sickness in pregnant women.
- Sold over-the-counter.
- Around 5.000 babies in Germany and 10.000 over the world:
  - born with *phocomelia (*malformation of the limbs),
  - only 50 % survived.
- Thalidomide was never approved by FDA in the USA, thanks to Ms. Frances Oldham Kelsey.
- Today, thalidomide is authorized, as an orphan drug, in a number of indications (cancer, leprosis).



- No medicinal product may be placed on the market unless it as been approved by the competent authorities.
- Authorization will only be granted if the:
  - safety
  - efficacy, and
  - quality

  of the medicinal products have been demonstrated by the person responsible for placing the product on the market.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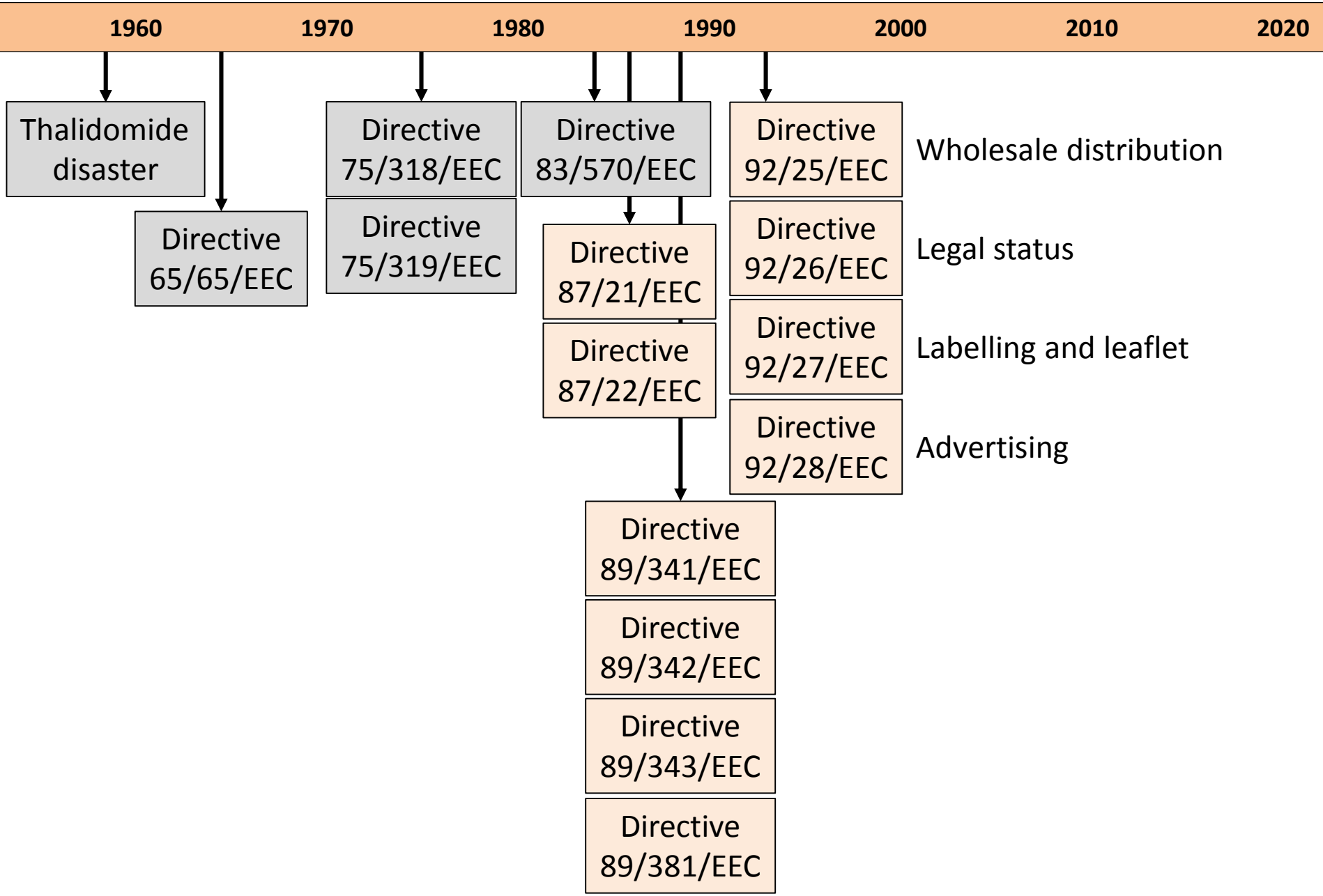
Thalidomide disaster
Directive 65/65/EEC
Directive 75/318/EEC
Directive 75/319/EEC
Harmonization of the analytical/toxicological/clinical protocols in respect of the testing of medicinal product.
Manufacturing authorization, good manufacturing practices and batch release.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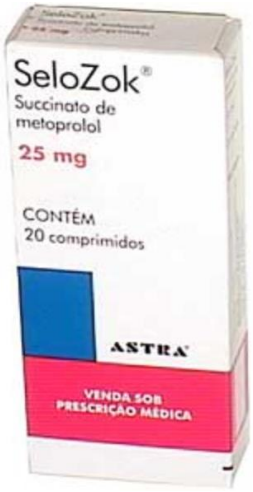
Directive 89/381/EEC
Directive 92/25/EEC
Directive 92/26/EEC
Directive 92/27/EEC
Directive 92/28/EEC
Wholesale distribution
Legal status
Labelling and leaflet
Advertising

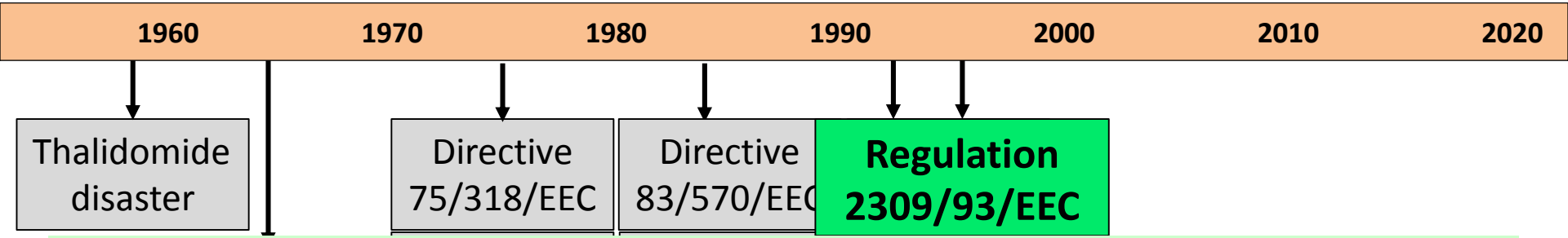
Early 90s: A fragmented European market for pharmaceuticals

- Despite the important harmonization effort, the pharmaceutical for pharmaceuticals was more fragmented than for any other consumer product.
- Marketing authorizations were still issued by national authorities.
  - Products were differing in all sorts of respects
    - Therapeutic indication
    - Instructions for use
    - Dosage
    - Colour
    - Pack size



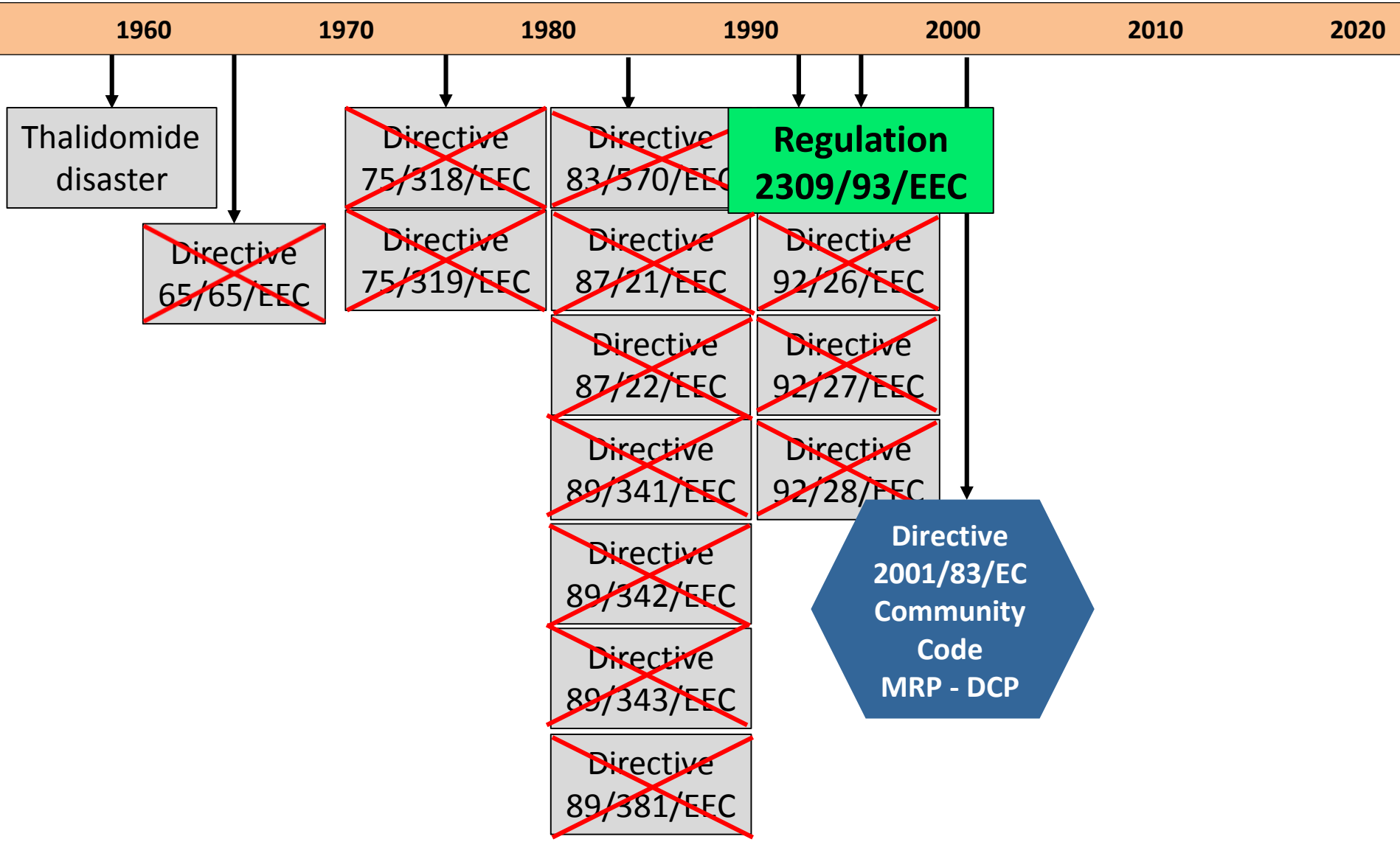
Early 90s: A fragmented European market for pharmaceuticals

- Despite the important harmonization effort, the pharmaceutical for pharmaceuticals was more fragmented than for any other consumer product.
- Marketing authorizations were still issued by national authorities.
  - Products were differing in all sorts of respects
  - Mutual recognition was not working
- Prices were differing widely between Member States as:
  - Some Member States were controlling price increases
  - Some Member States were controlling prices
  - Some Member States were controlling profits
  - All Member States were controlling reimbursements by their national health service.
- Parallel imports were florishing (protected by the European Commission and the European Court of Justice.
- To combat parallel imports, producers were accentuating product differentiation.



1995 : a new EU authorization system for medicinal products

- Creation of the European Medecines Agency (EMA) seated in London.
- Creation of an EU centralized procedure:
  - Single application to EMA
  - Single authorization granted by the European Commission
  - Same product commercialized throughout the EU
- Creation of:
  - Decentralized procedure
  - Multistate procedure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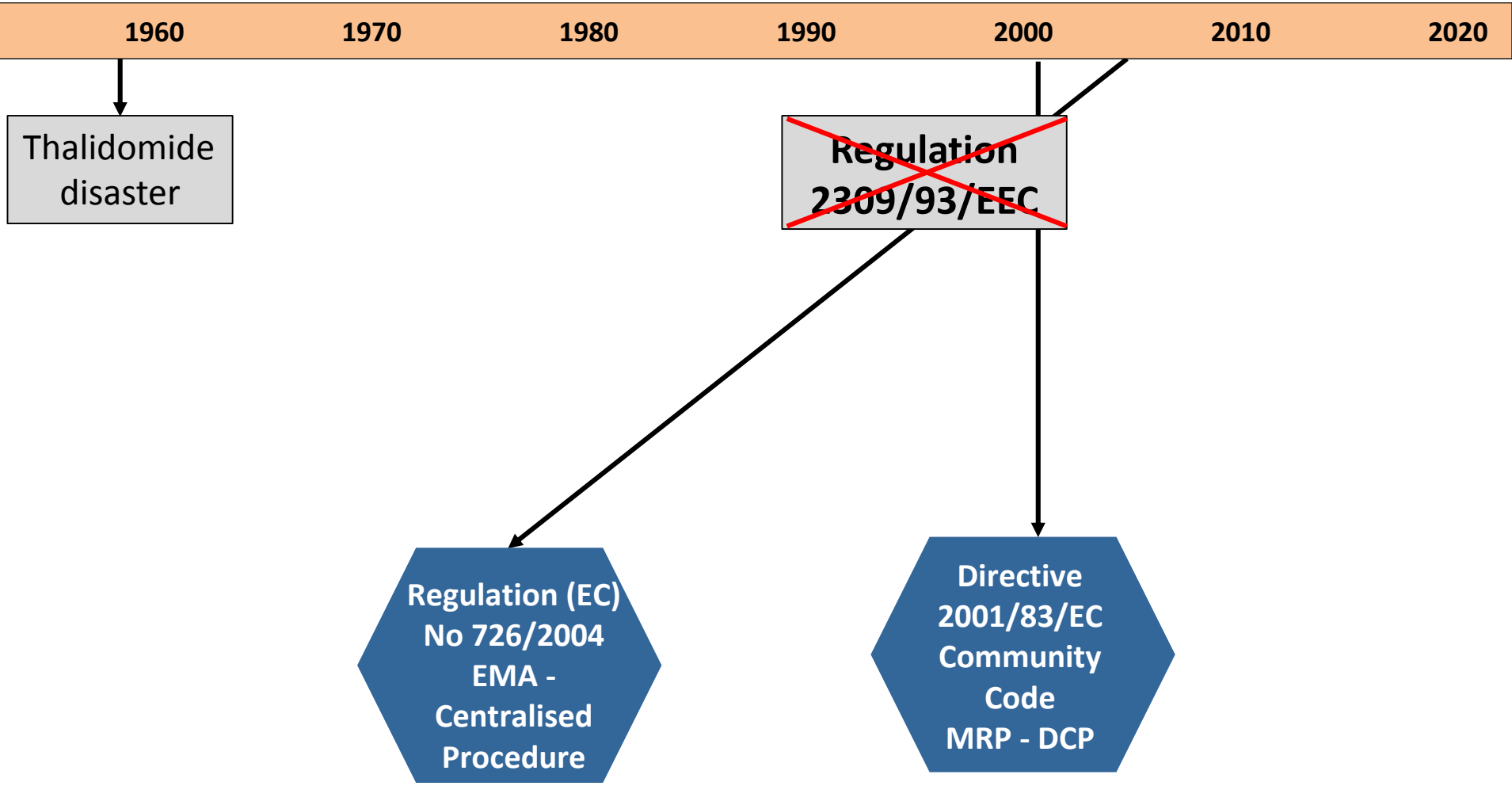
Directive 2001/83/EC Community Code MRP - DCP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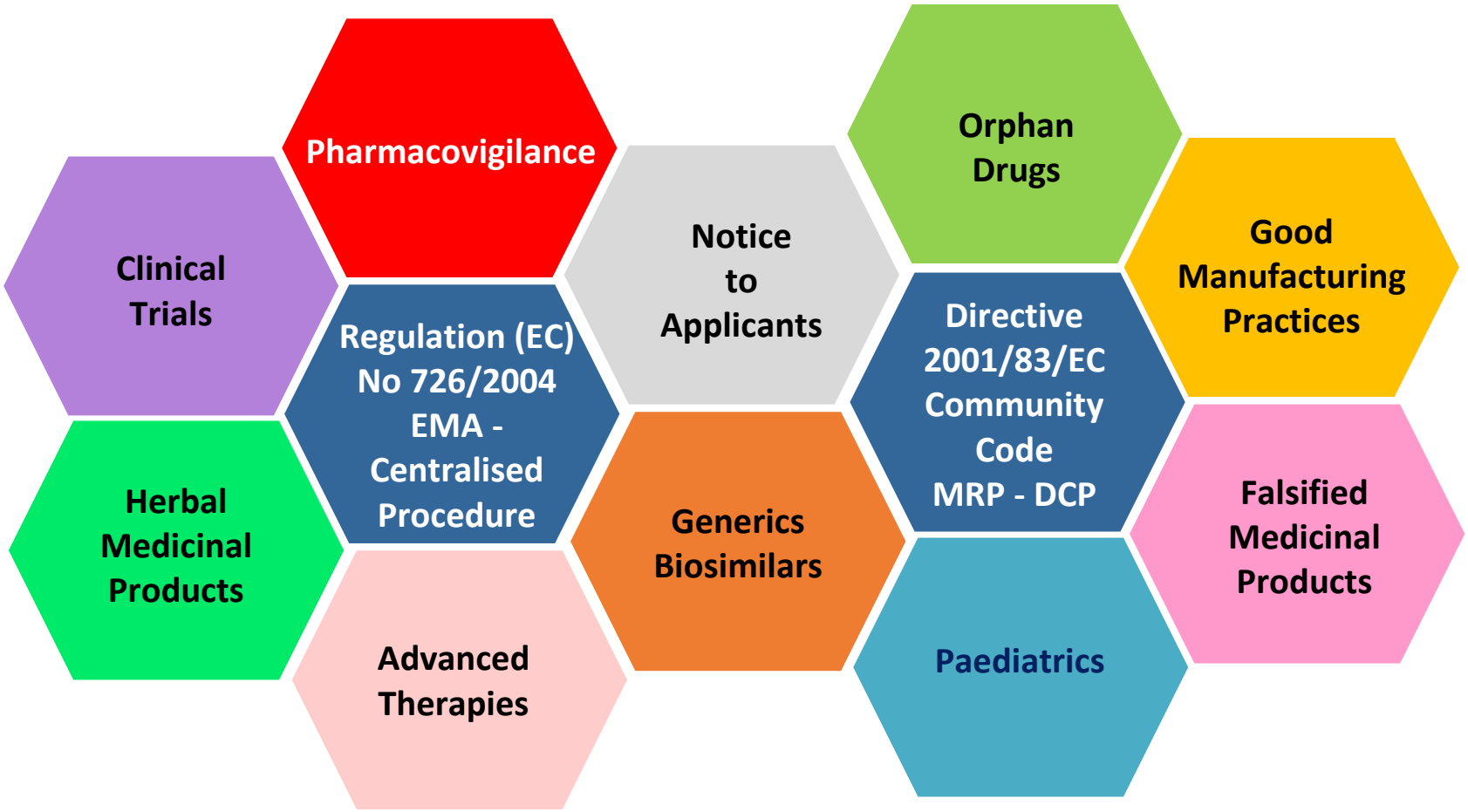
Thalidomide disaster
Regulation 2309/93/EEC
Regulation (EC) No 726/2004 EMA - Centralised Procedure
Directive 2001/83/EC Community Code MRP - DCP

1960 1970 1980 1990 2000 2010 2020

EU Pharmaceutical Law



❑ Key Principles of EU Pharmaceutical Law

Objectives

Protection of public health

Free movement of medicinal products within the EU

1960 1970 1980 1990 2000 2010 2020

❑ Key Actors

LEGISLATION

Proposal:

European Commission

→

European Council

+

European Parliament

Adoption:

Implementing Acts:

European Commission

+

Committee of EU MSs

Interpretation:

European Court of Justice

1960 1970 1980 1990 2000 2010 2020

❑ Key Actors

AUTHORIZATIONS

Centralised Procedure

Application to:

European Medicines Agency EMA

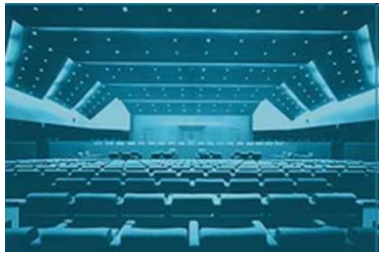
Decision:

European Commission

+

Committee of EU MSs

Appeal:



European Court of Justice

❑ Marketing Authorizations

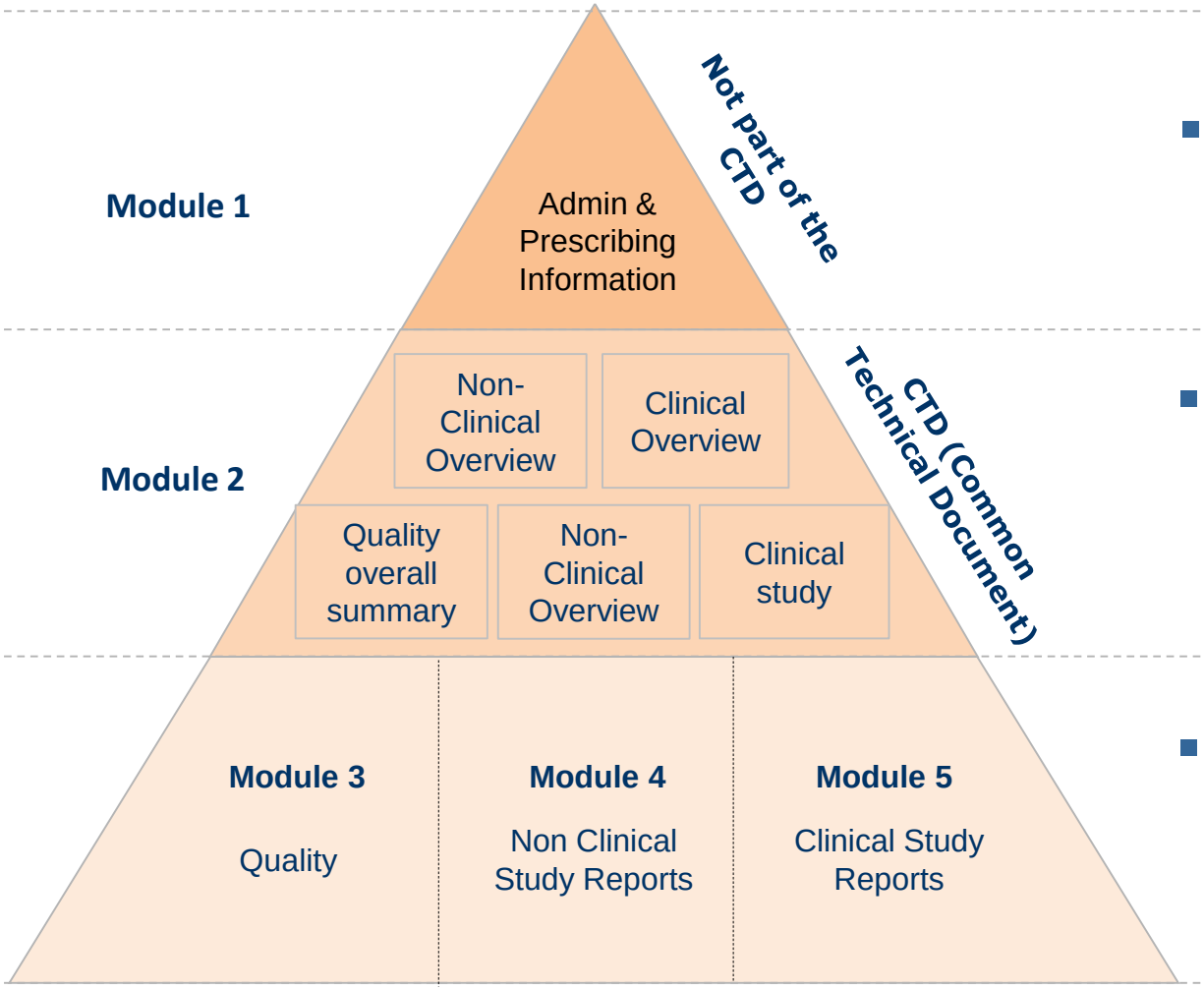
A medicinal product may only be placed on the market in the European Union when a **marketing authorisation** has been issued:

- 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

1960 1970 1980 1990 2000 2010 2020

❑ 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.

❑ 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?

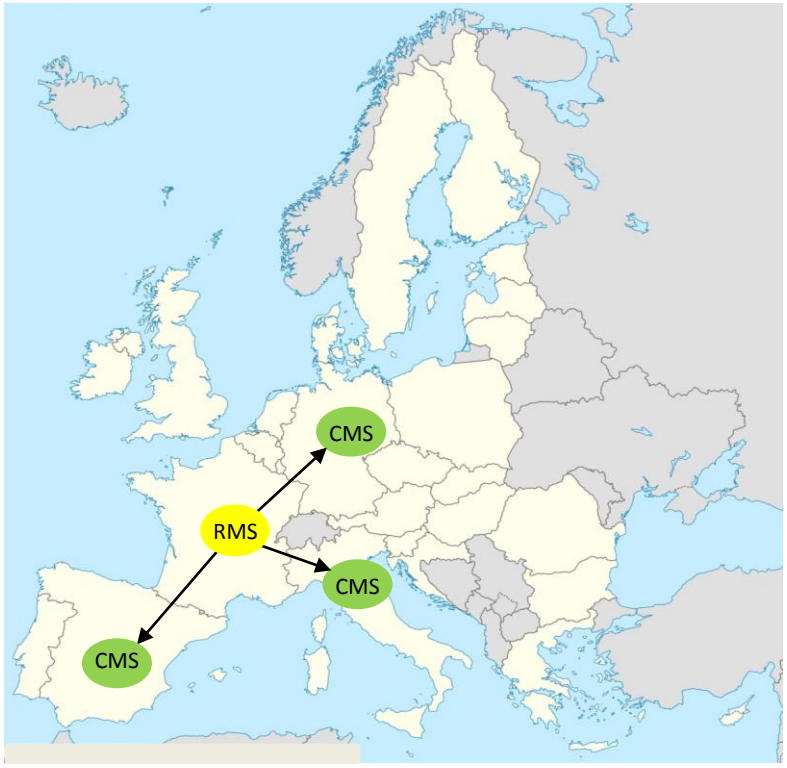
Depends on:

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

1960 1970 1980 1990 2000 2010 2020

❑ Mutual Recognition Procedure (MRP)

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

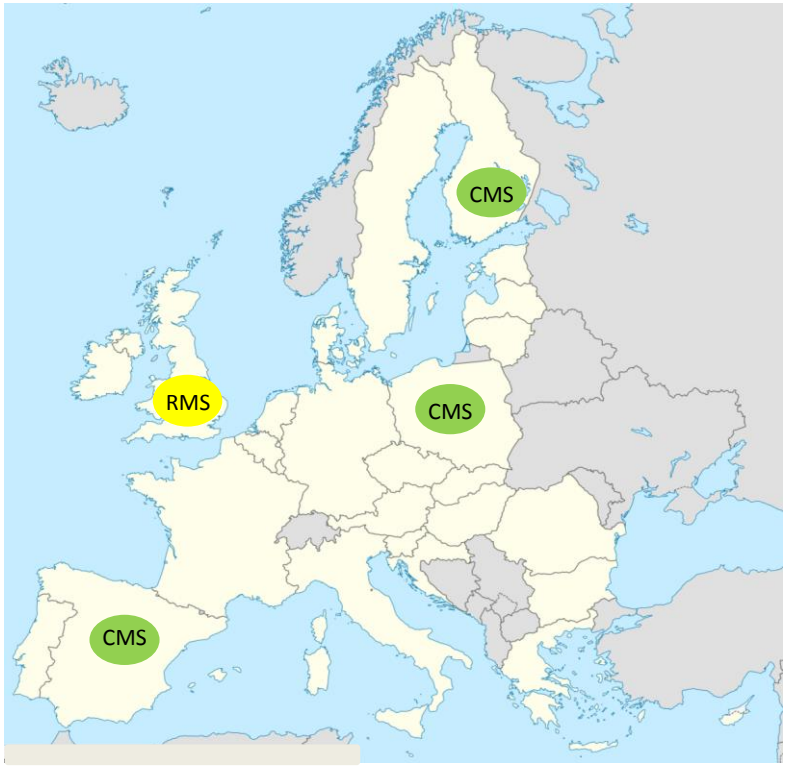


- Starts from an **already existing national marketing authorisation** granted by one Member State – the **Reference Member State (RMS)**
- One or more Member States – the **Concerned Member States (CMS) –** are asked to **recognize** the authorization granted by the Reference Member State.
- In case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

1960 1970 1980 1990 2000 2010 2020

❑ Decentralised Procedure (DCP)

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).

1960 1970 1980 1990 2000 2010 2020

❑ Centralised Procedure (CP)

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

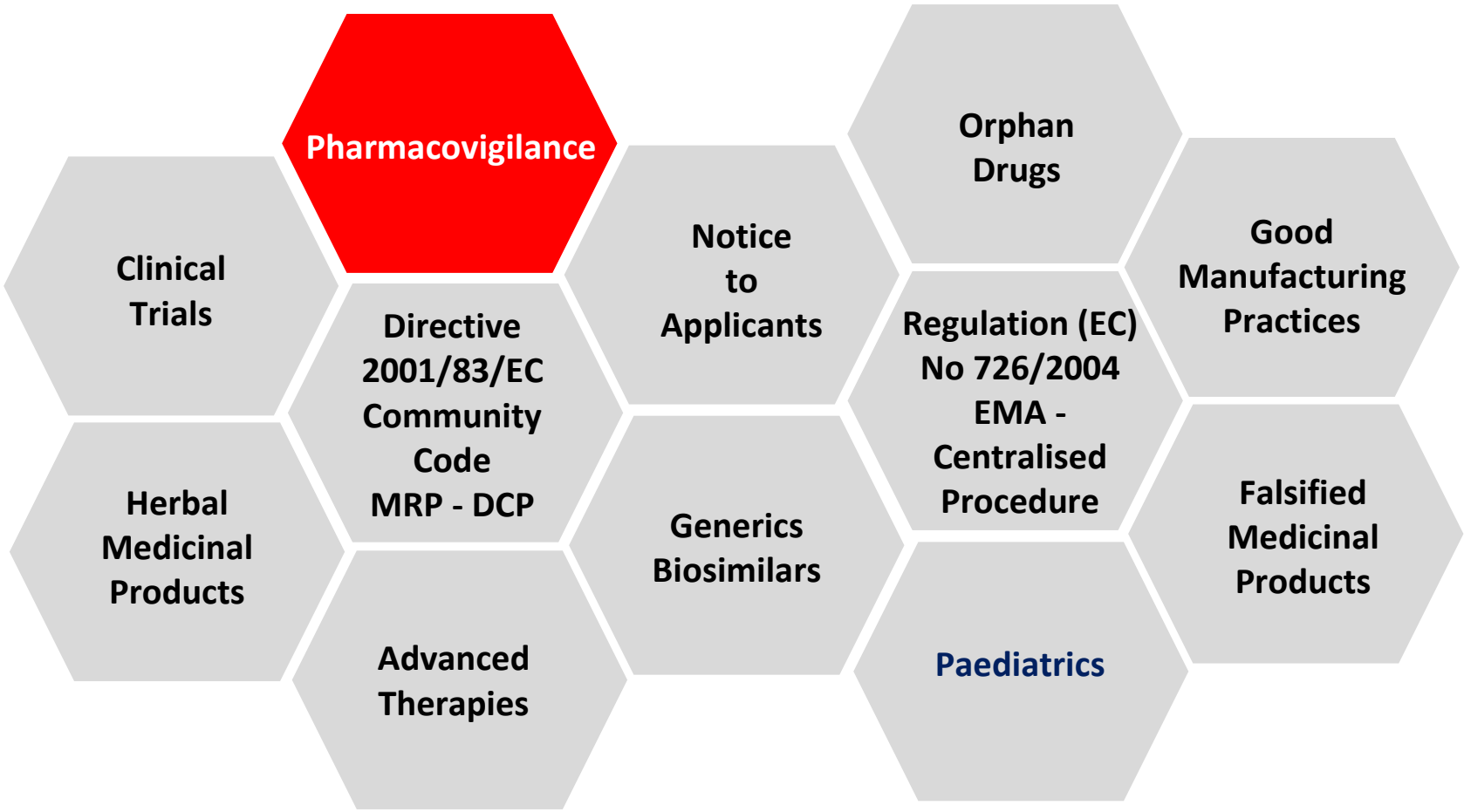
- Single application to place the product on the market throughout the European Union.

- 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

1960 1970 1980 1990 2000 2010 2020

EU Pharmaceutical Law



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

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

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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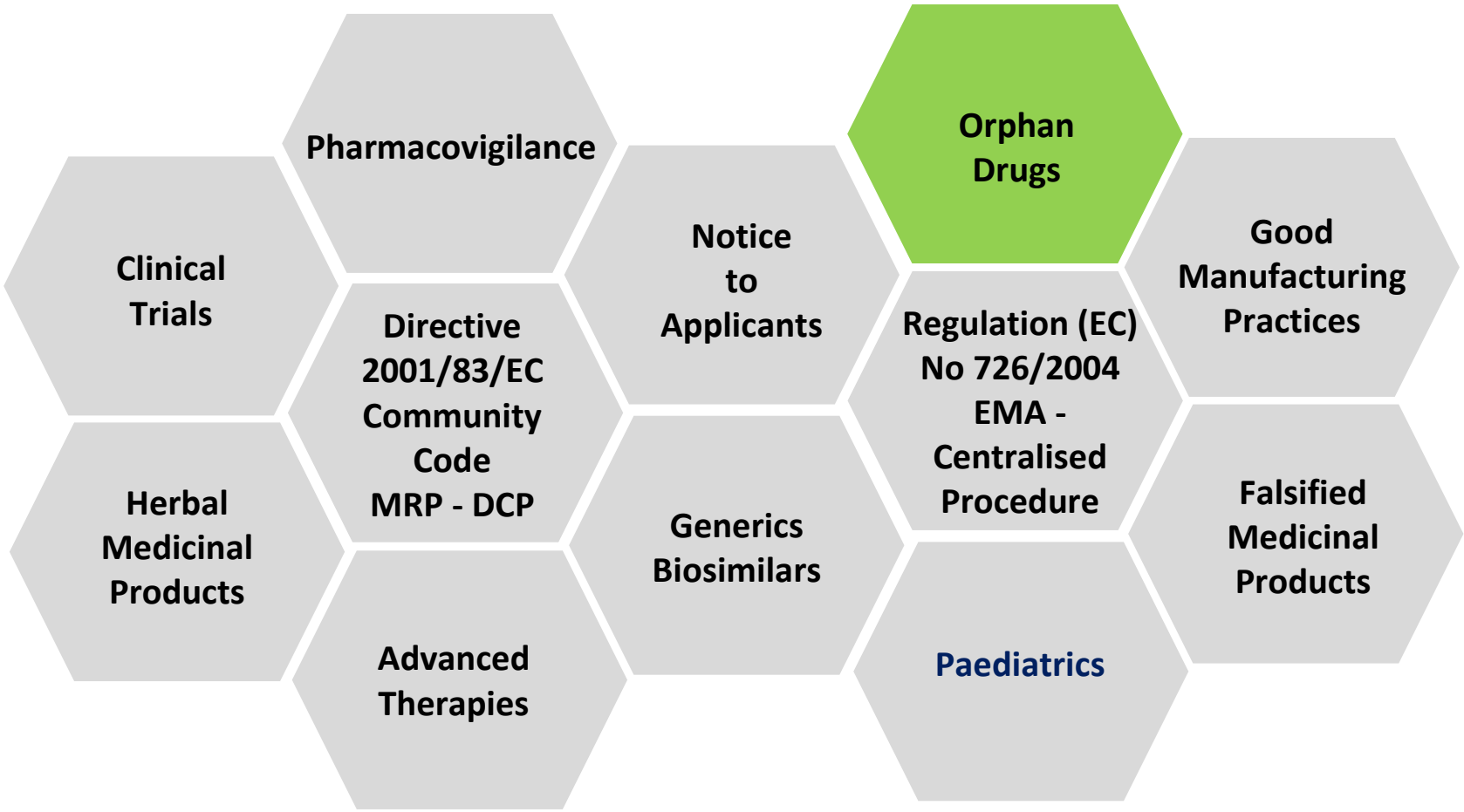
EU Pharmaceutical Law



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

Orphan Drugs

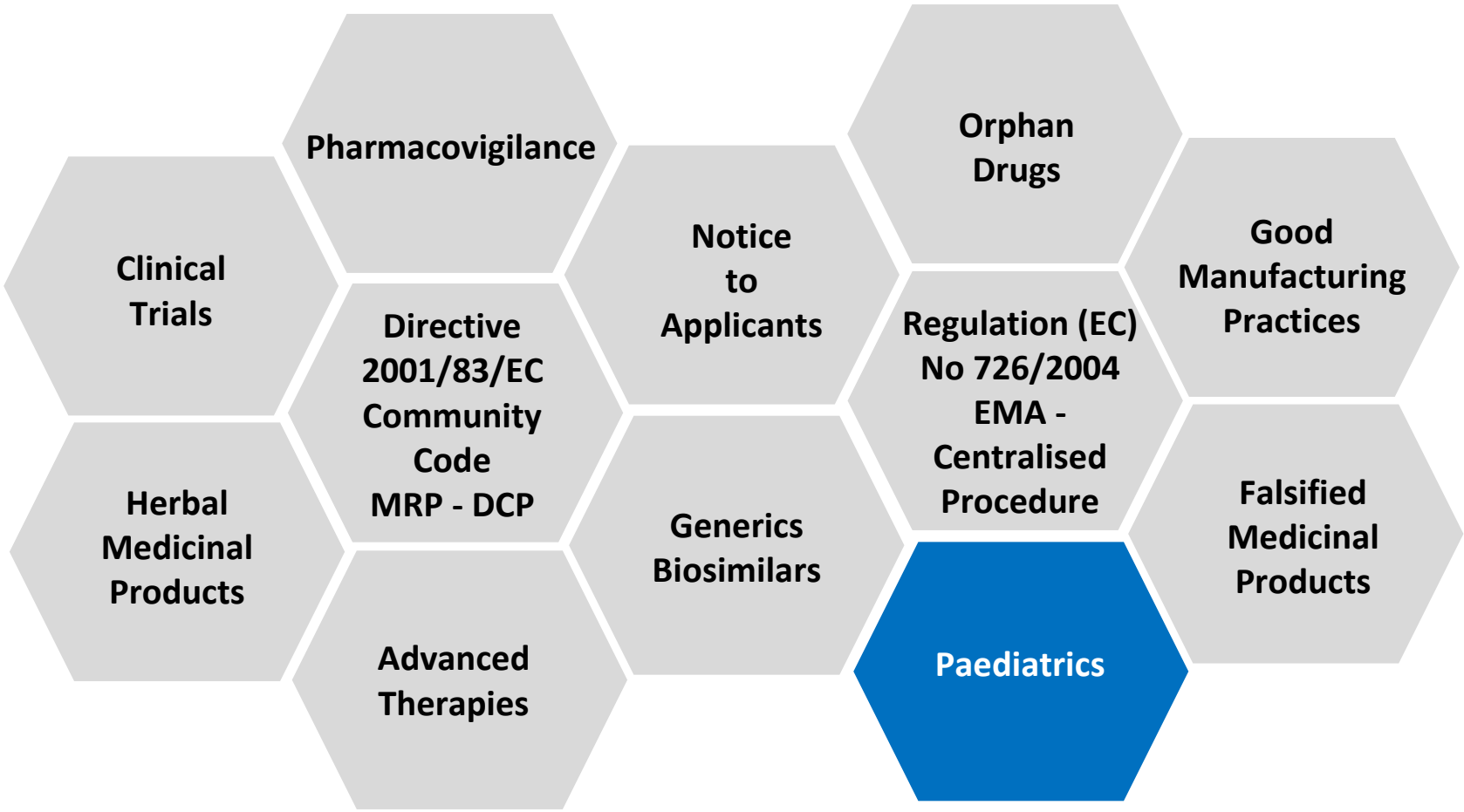
Regulation (EC) No 141/2000

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

1960 1970 1980 1990 2000 2010 2020

EU Pharmaceutical Law



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

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

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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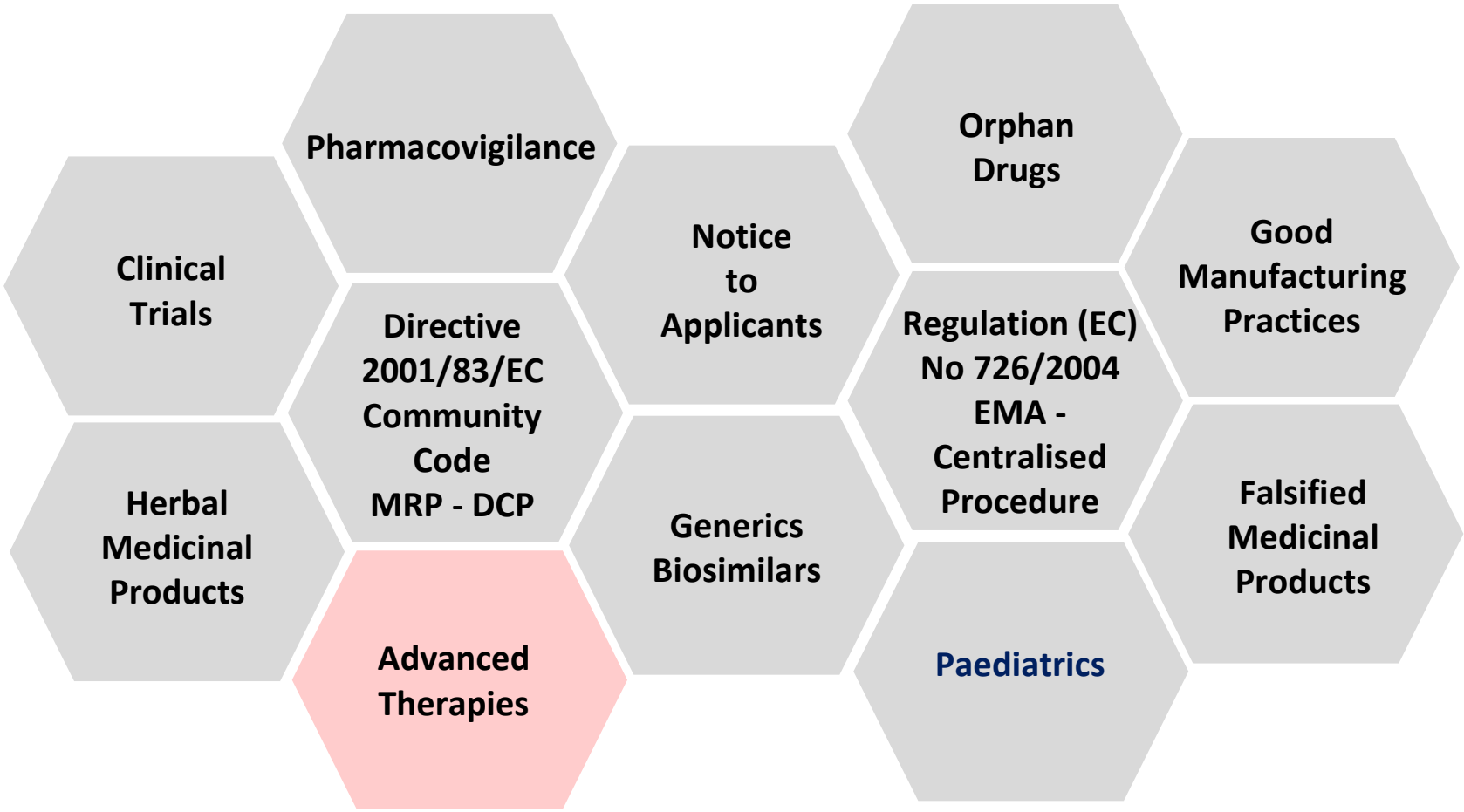
EU Pharmaceutical Law



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.

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!