EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Marketing Authorisation Routes in the EU

The EU medicines regulatory system and the European Medicines Agency: an introduction for international regulators and non-governmental organisations
18 September 2017

Presented by Maria Nieto-Gutierrez
Procedure Management Department

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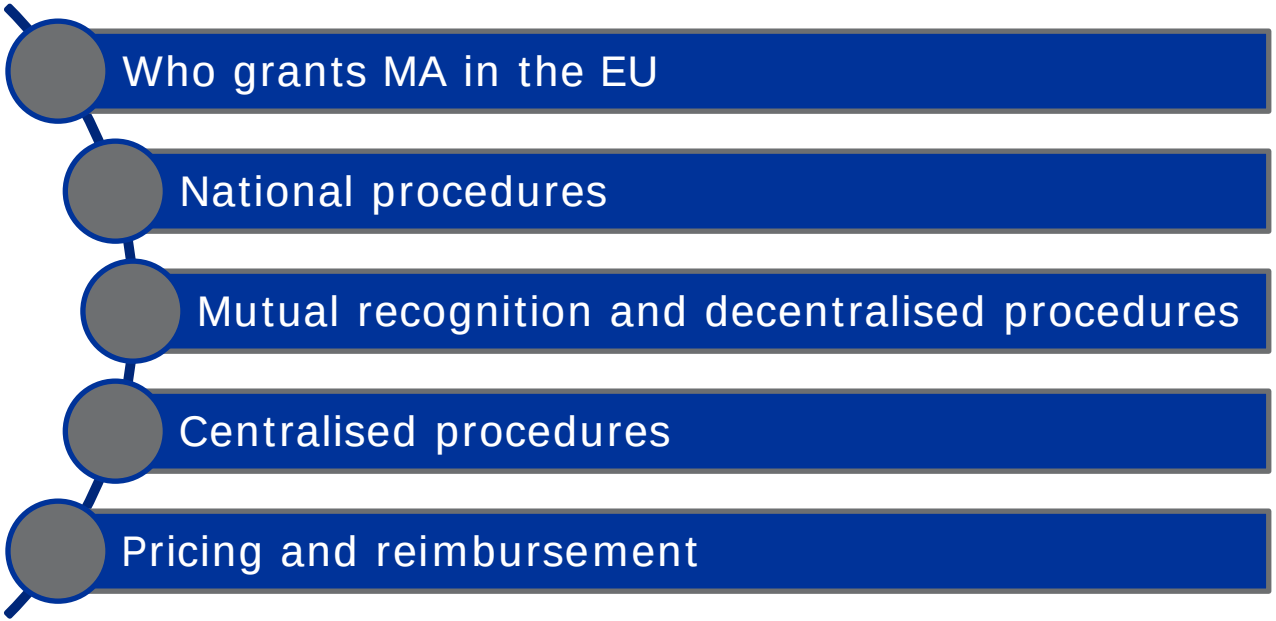
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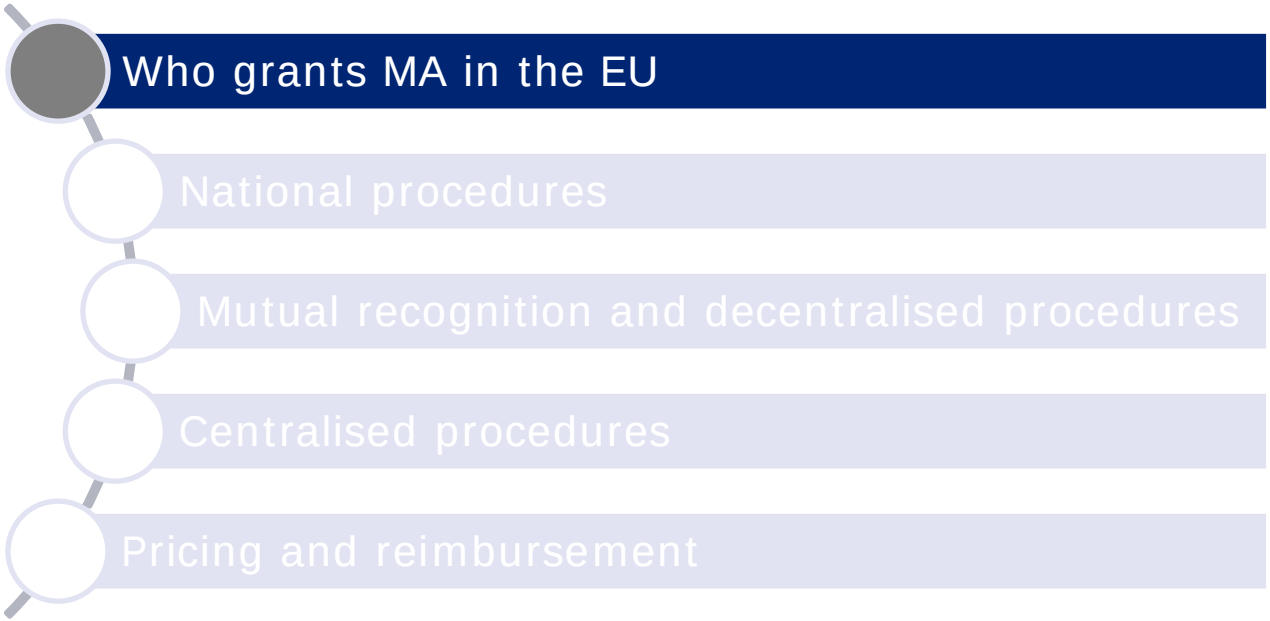
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Who grants a MA in the EU?

- To protect public health and ensure the availability of high quality, safe and effective medicines for European citizens, **all medicines must be authorised** before they can be placed on the market in the EU.
- 50 years of **EU pharmaceutical legislation**
  - ❖ In 1965 the first EU law on medicinal products was adopted
  - ❖ Progressive harmonisation of requirements for the granting of marketing authorisations and post-marketing monitoring has been implemented across the entire EU
- The **data requirements** and standards governing the authorisation of medicines are the same in the EU.

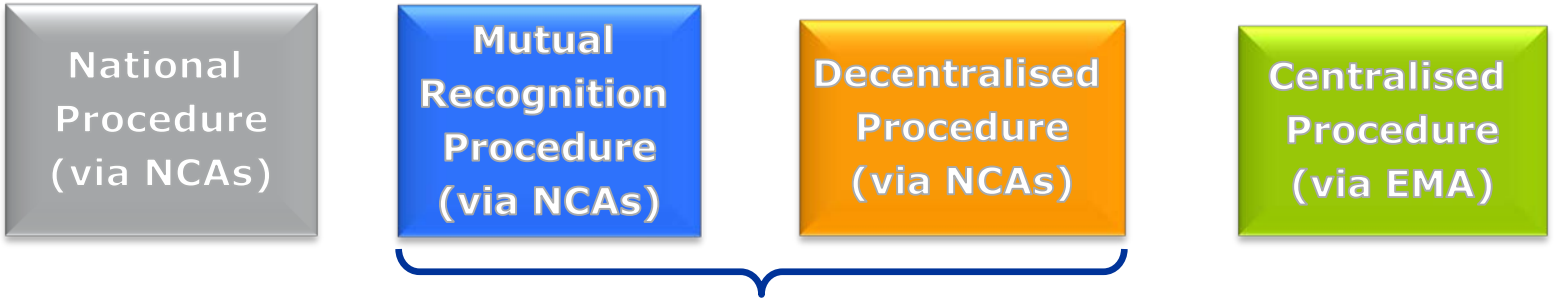
Who grants a MA in the EU?

Different authorisation routes: one set of common rules

National procedures (via NCAs)

Centralised procedure (via EMA)

Who grants a MA in the EU?

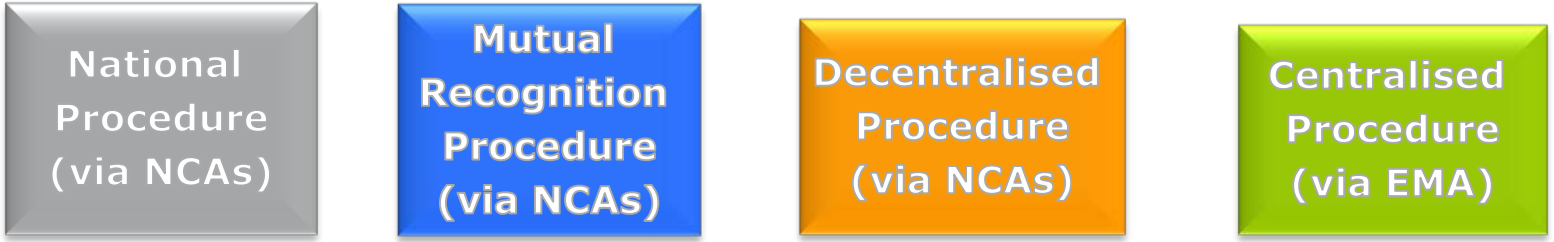


Authorisation by a single MS

Authorisation by several MSs, based on assessment by Reference MS

Authorisation by European Commission, based on assessment by EMA, valid in all MSs

Who grants a MA in the EU?



Depending on:

- Type of product
- Authorisation history in EU
- Regulatory & marketing strategy

Different authorisation routes: one set of common rules

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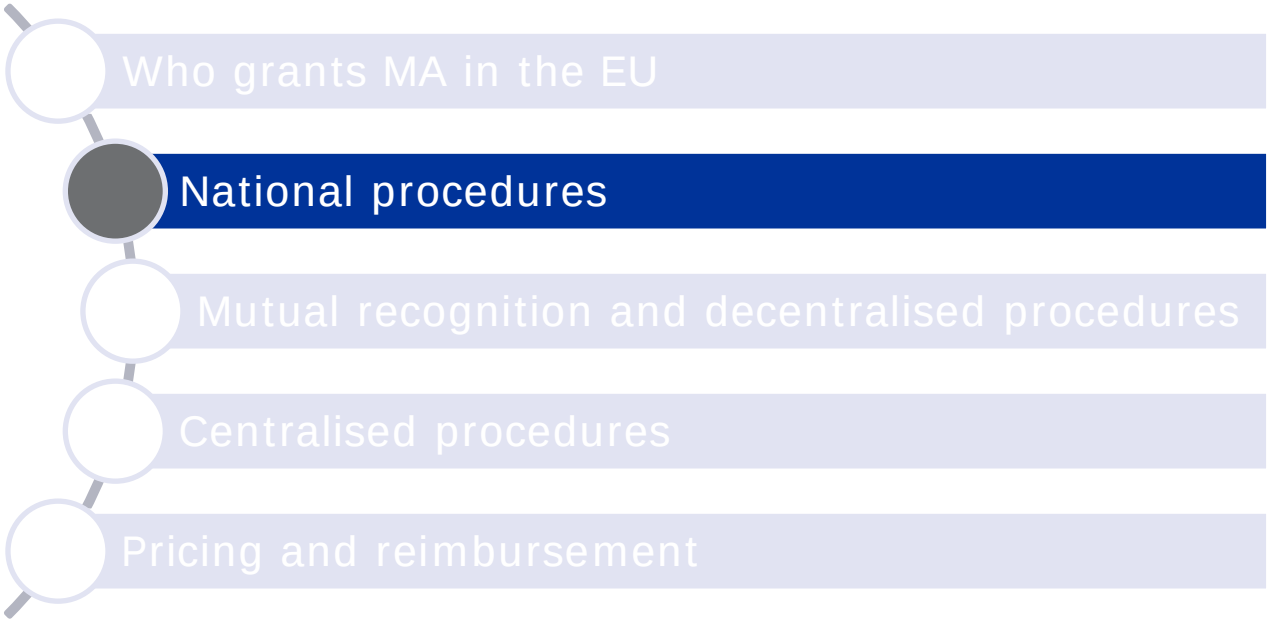
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National procedures

- The majority of medicines available in the EU are authorised at national level:
  - Authorised before EMA creation
  - Not in the scope of the centralised procedure

- Each EU Member State has its own national authorisation procedures

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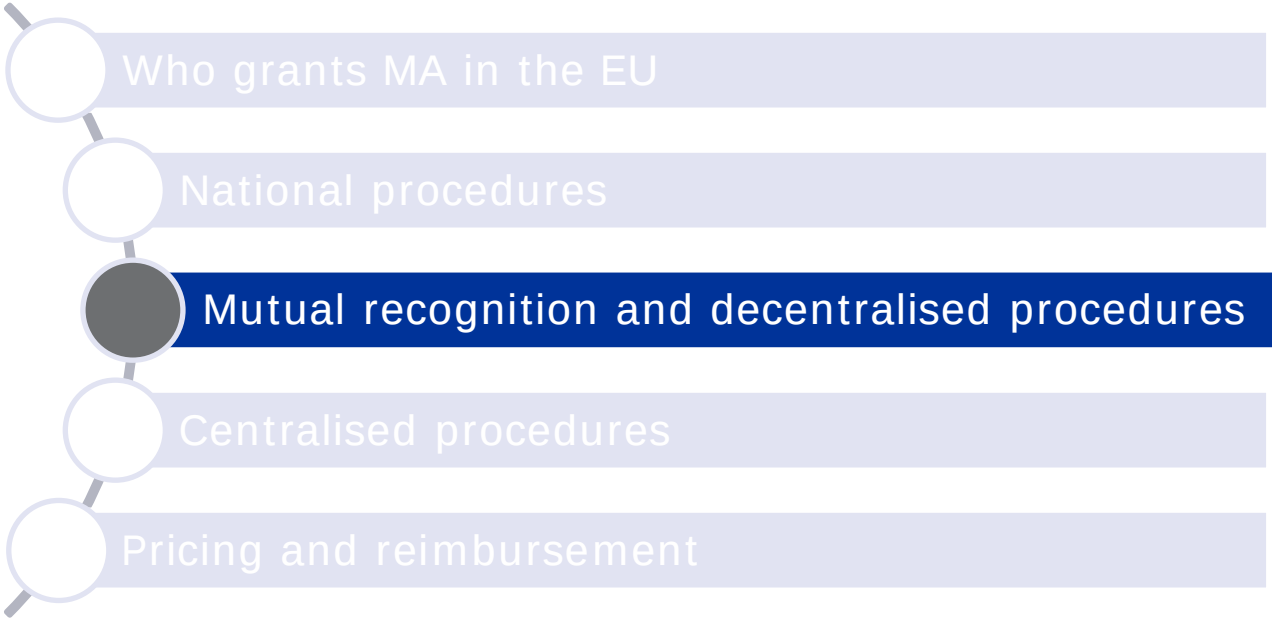
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Mutual recognition procedures (MRP)

- Principle of recognition of an <u>already existing</u> national MA by one or more EU Member States

Allows Member States to rely on each other's scientific assessments.

Decentralised procedure (DCP)

- No existing MA in the EU

Simultaneous authorisation in more that one Member State

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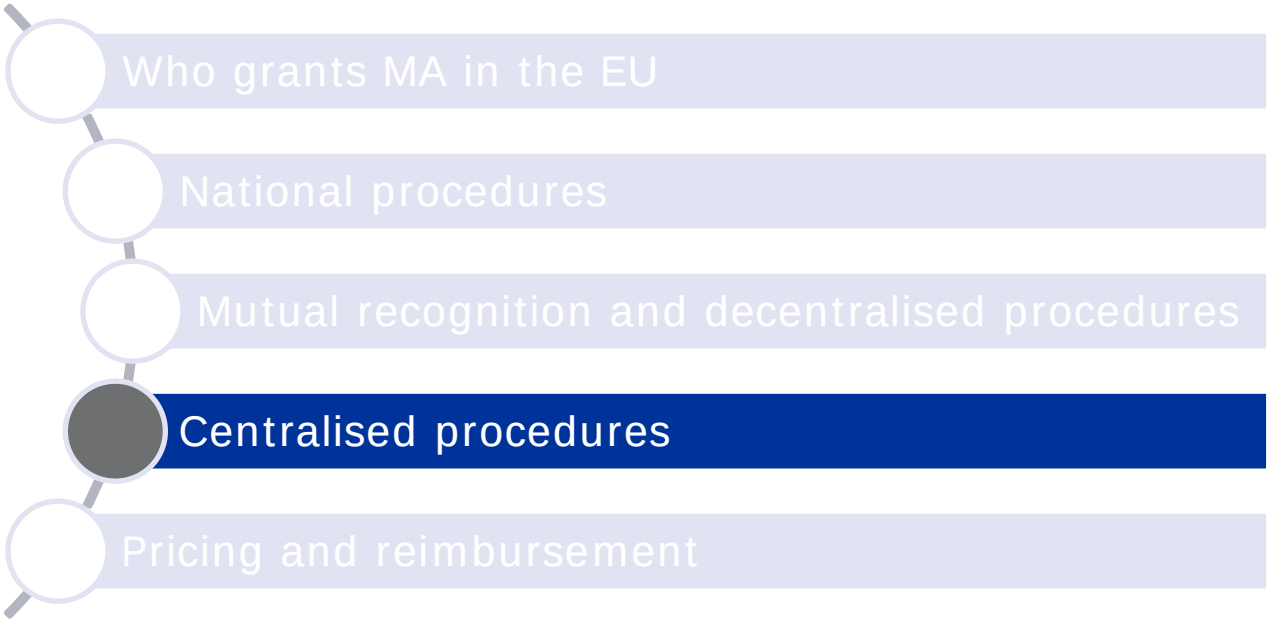
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Centralised procedures

- **One single MA application** to EMA
- Compulsory for most innovative medicines, including rare diseases.
- **One assessment** procedure (scientific committee's opinion) based on individual assessments by Member States
- Common decision making process (one European Commission decision)
- **One MA valid in all EU member states and EEA**
- Transparent evaluation

What is the benefit of the centralised procedure for EU citizens?

- Medicines are authorised for all EU citizens at the same time
- Centralised safety monitoring
- Product information available in all EU languages at the same time

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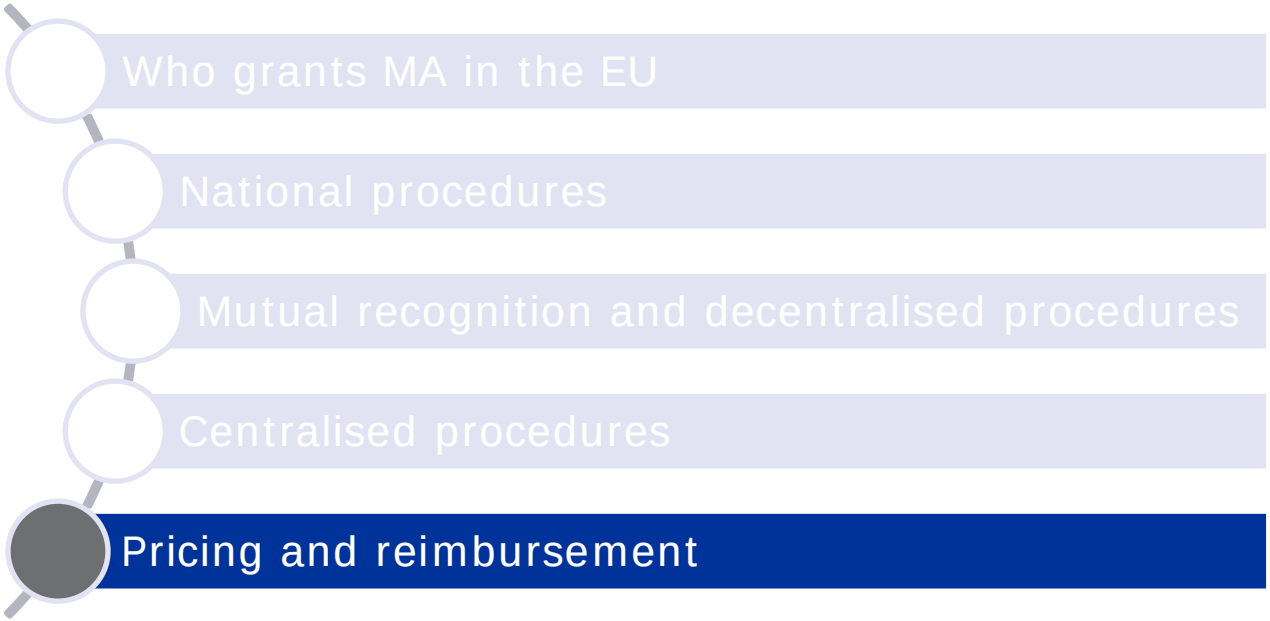
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Pricing and reimbursement

- **Health technology assessment (HTA) bodies** provide recommendations on medicines that can be financed or reimbursed by the healthcare system in a particular EU Member State or region.
- The assessment criteria used by HTA bodies differ between EU Member States, in accordance with regional and national legislation.
- **The EMA has been working closely with HTA bodies since 2008.**

  EMA offers consultations in parallel with European Network for Health Technology Assessment (EUnetHTA) as of July 2017. The procedure is a single gateway for parallel consultations with EMA, EUnetHTA and HTA bodies on their evidence-generation plans.
- A **close interaction** between regulators, HTA bodies and other relevant bodies is critical to enable patients' access to important new medicines.

Any questions?

Further information

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The role of EMA

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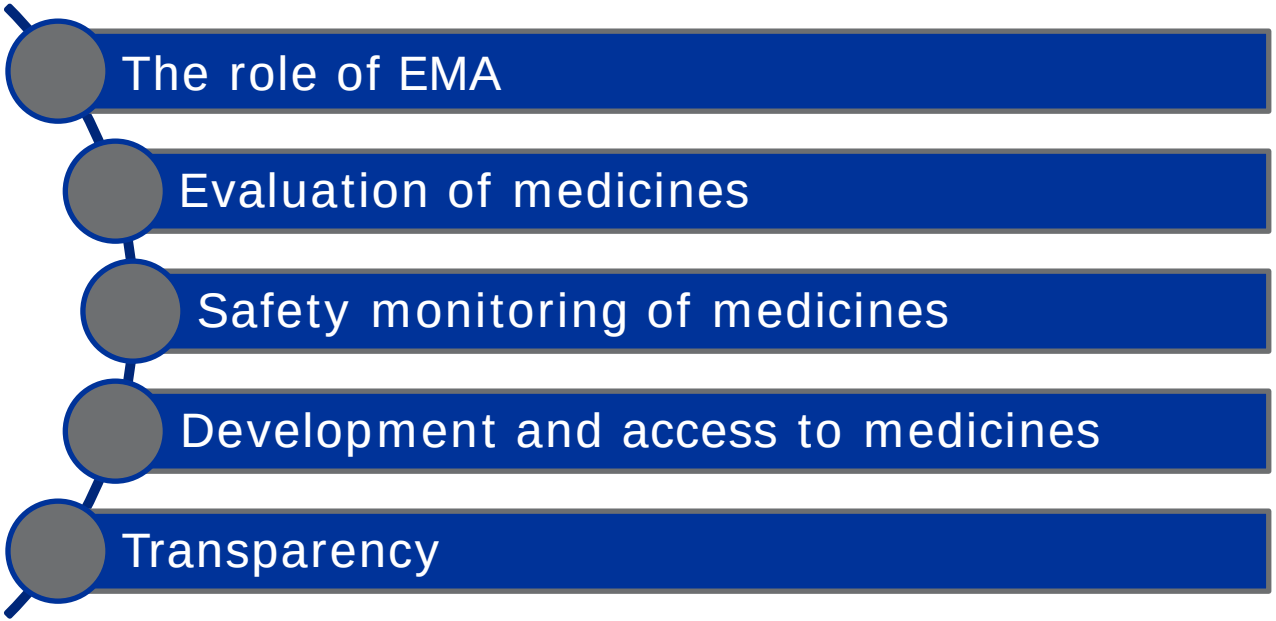
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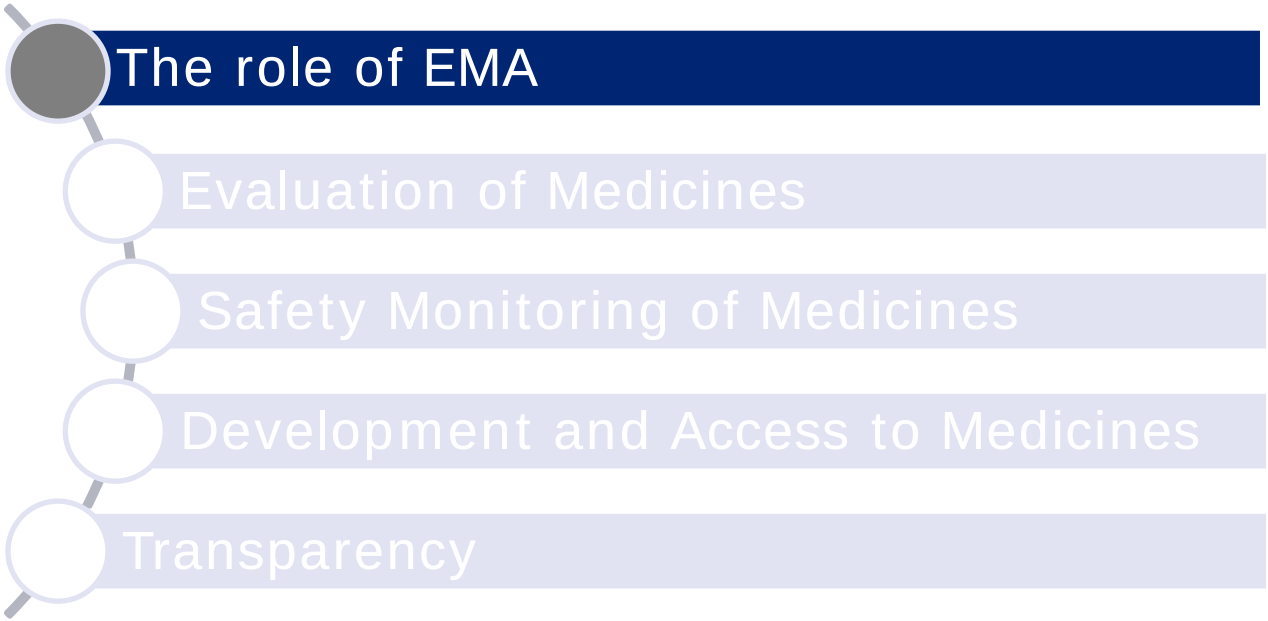
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The role of EMA

- Decentralised **agency of the EU**
- Founded in **1995**
- Located in London until March 2019
- **Reg. (EC) No 726/2004**
  [previously Reg. (EEC) No 2309/93/EC]
- Scientific secretariat responsible for **coordinating** the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products*

* Art. 55 of Reg. (EC) No 726/2004

The role of EMA

Who do we work for?

over **500** million people living in the European Union

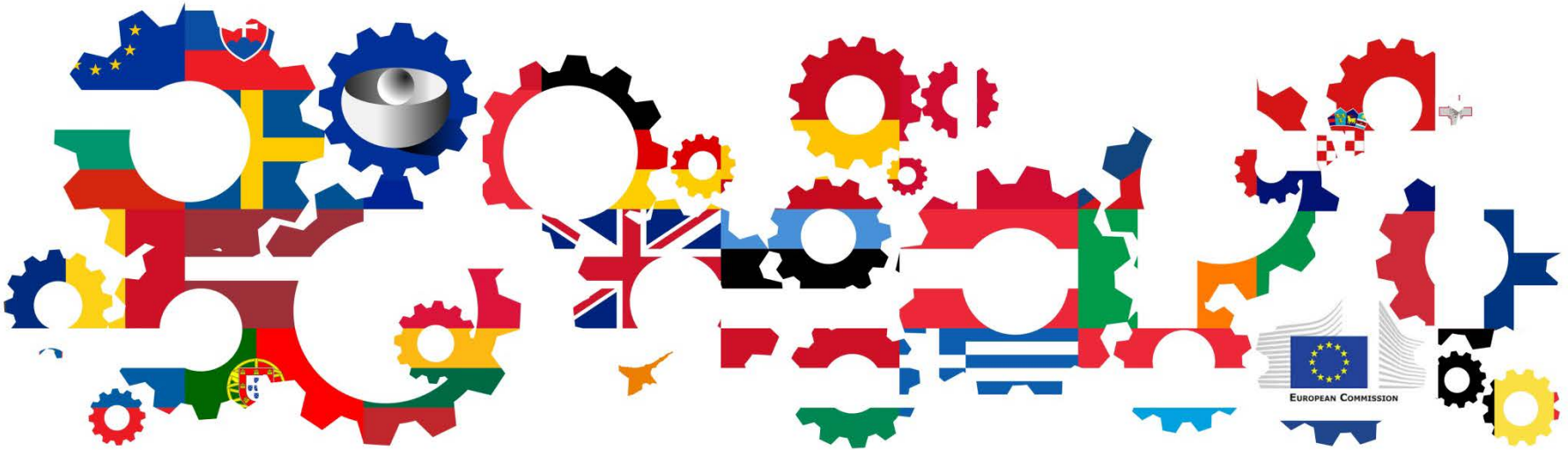
28 member states

27% of global sales of medicines

24 official languages

The role of EMA

Who do we work with?



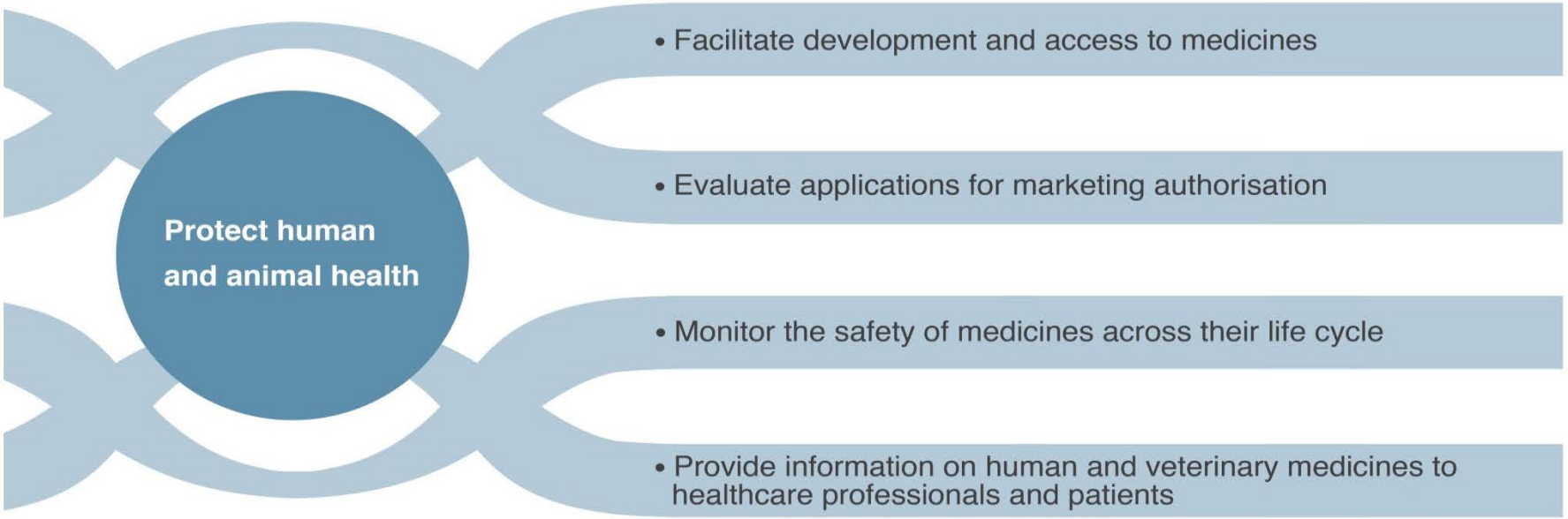
~ 50 national regulatory authorities

European Commission

European Medicines Agency

The role of EMA

What do we do?



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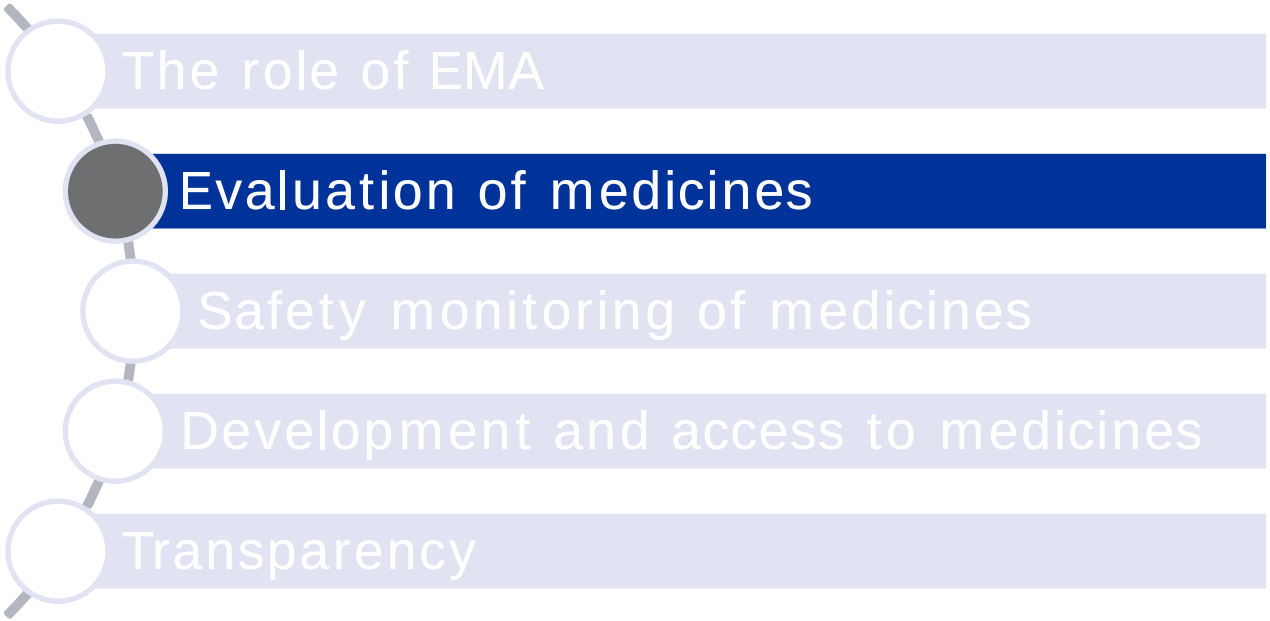
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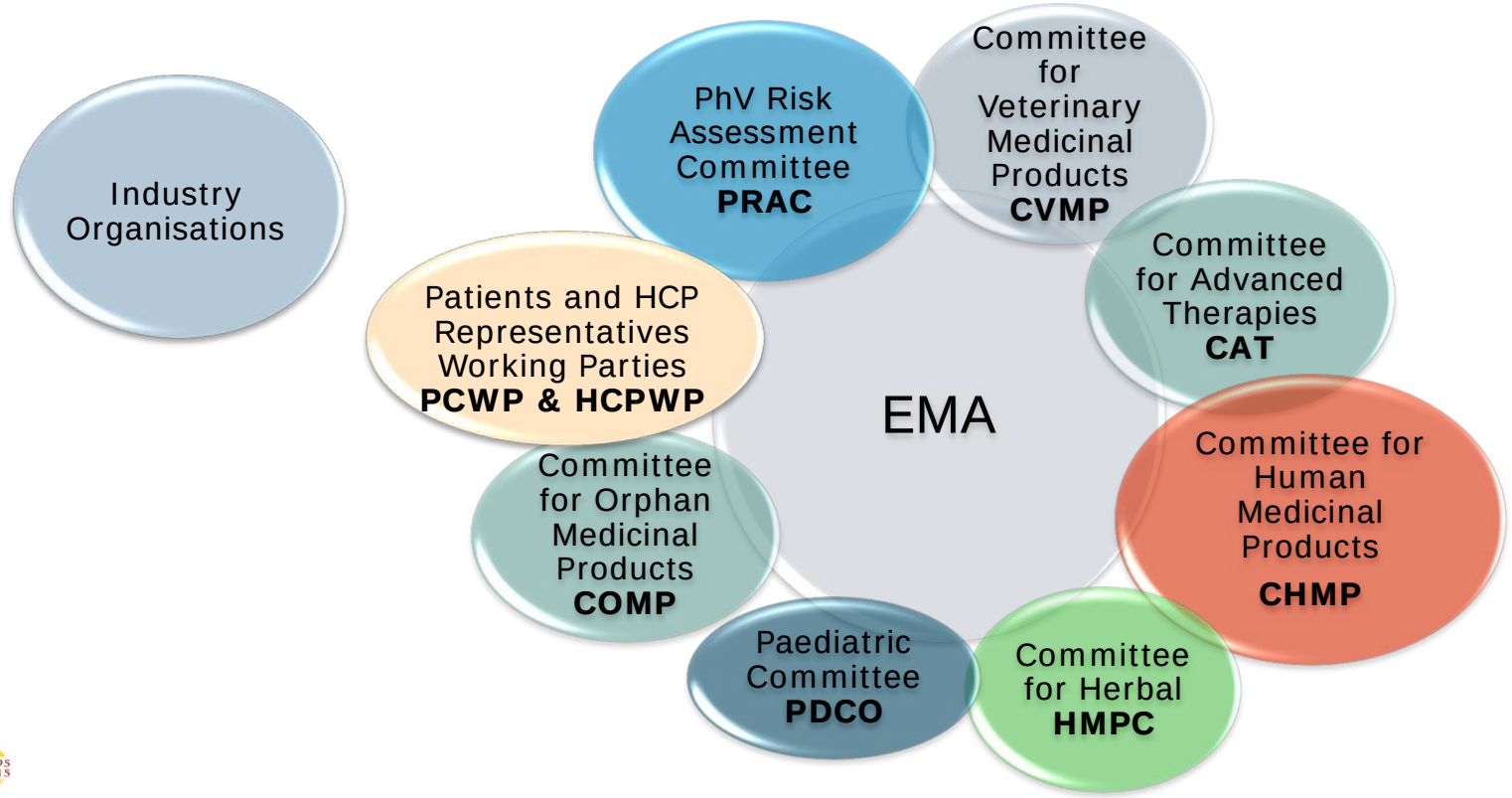
Evaluation of medicines

- The EMA's **scientific committees** provide independent recommendations on medicines for human and veterinary use, based on a comprehensive scientific evaluation of data.
- **EU experts** participate in the work of EMA as members of its scientific committees, working parties, scientific advisory groups, or as members of the national assessments teams that evaluate medicines.
- Increasingly, **patients and healthcare professionals** (HCP) are involved in the work of the Agency including evaluation of medicines.
- By **working together**, Member States reduce duplication, share the workload and ensure an efficient and effective regulation of medicines across the EU.

The EMA's scientific committees



The EU experts

- **Diversity:** Exchange of knowledge, ideas and best practise striving the highest scientific standards.
- **Impartiality**: EMA policy on Handling Conflicts of Interest. Public Declaration of Interest.

Composition of scientific committees:

- 1 member + 1 alternate nominated by each of the 28 EU MS
- 1 member + 1 alternate from NO and IS (observers)
- Co-opted members for specific expertise on scientific or technical matters
- Elected Chair and Vice-Chair
- 3 years renewable mandate

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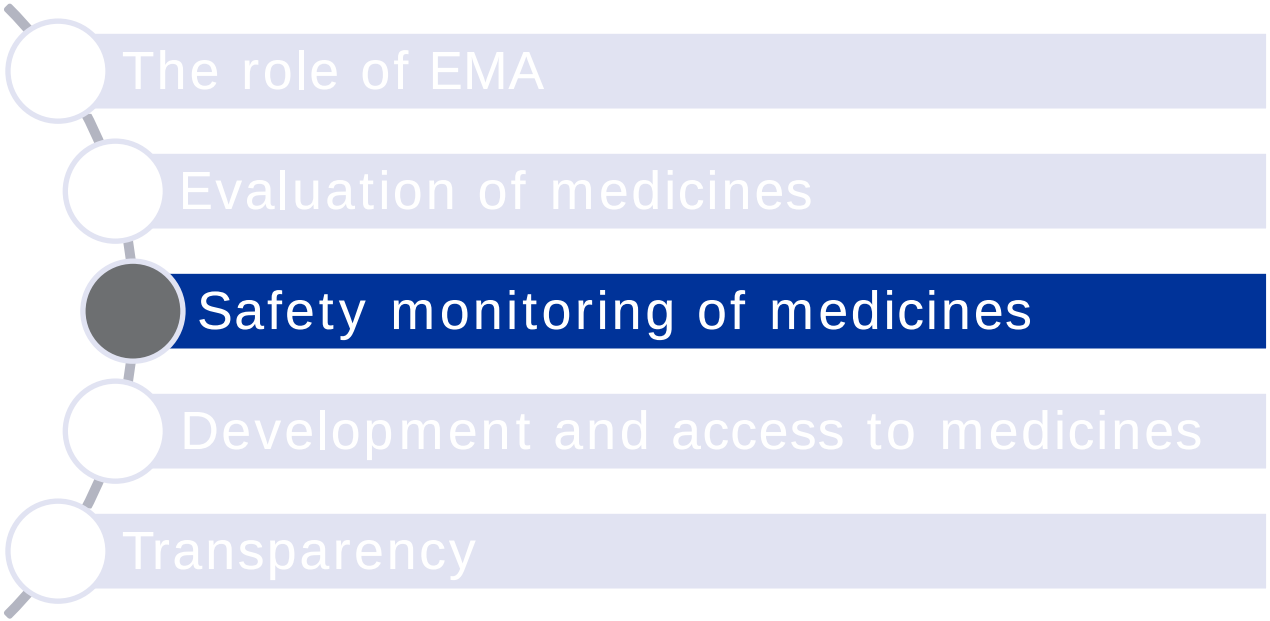
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Safety monitoring of medicines

- EMA continuously monitors and supervises the safety of medicines that have been authorised in the EU, to ensure that their benefits outweigh their risks.
- The **Pharmacovigilance Risk Assessment Committee (PRAC)** of EMA is dedicated to the safety of medicines.
- EMA coordinates the **EU pharmacovigilance system** and operates services and processes to support pharmacovigilance in the EU.
- EMA operates **Eudravigilance**, an EU web-based information system that collects, manages and analyses report of suspected side effects of medicines.
- **Public hearings** are now a tool available during EU safety reviews of medicines.

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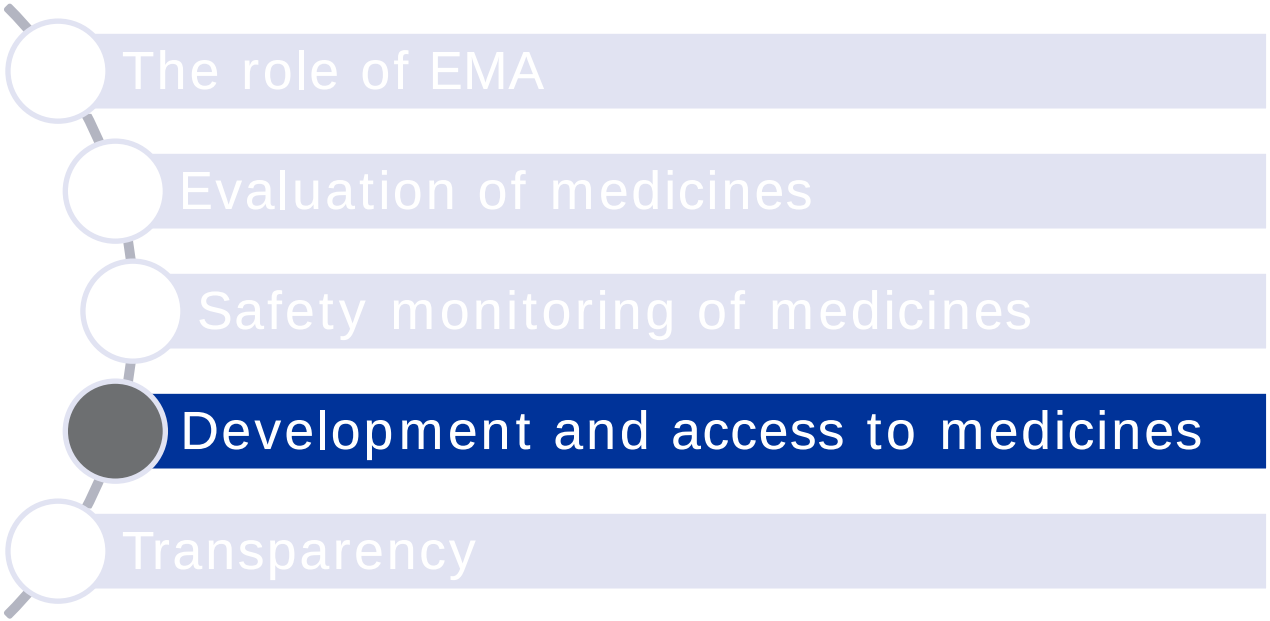
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Development and access to medicines

- EMA is committed to enabling **timely patient access** to new medicines, and plays a vital role in supporting medicine development for the benefit of patients.
- EMA prepares **scientific guidelines** on requirements for the quality, safety and efficacy testing of medicines, reflecting the latest thinking on developments in biomedical science.
- EMA provides product-specific **scientific advice** through the Scientific Advice Working Party (SAWP).
- EMA supports **research and innovation** in the pharmaceutical sector, and promotes innovation and development of new medicines by European micro-, small- and medium-sized-enterprises.

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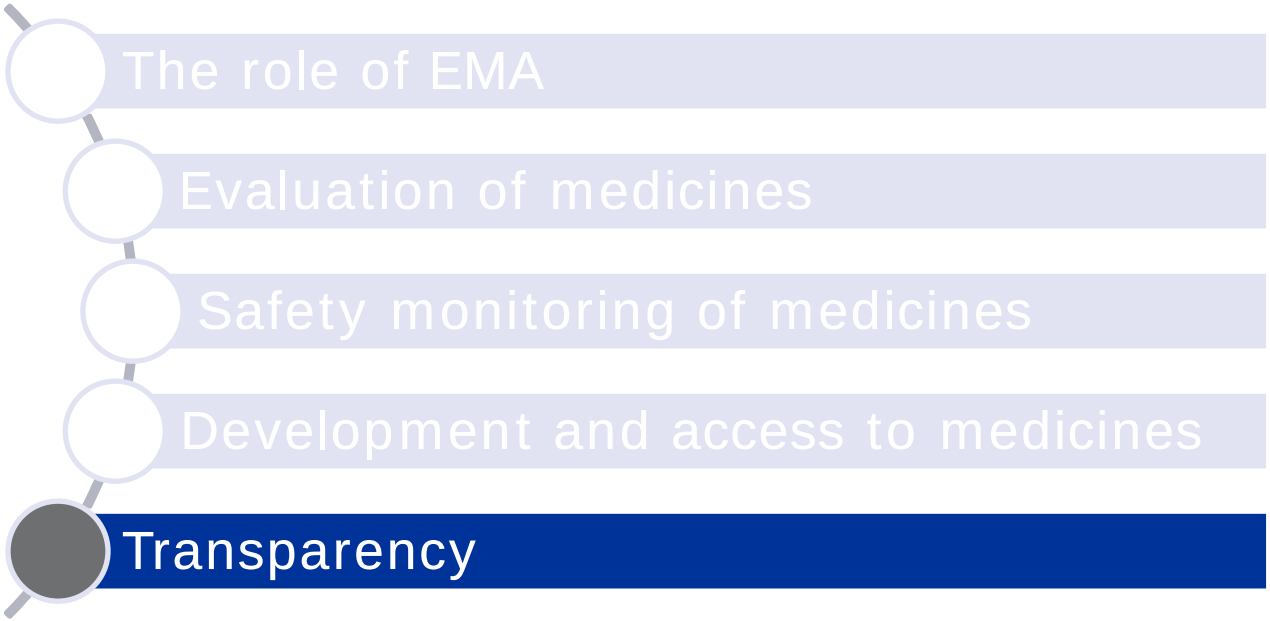
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Transparency

- EMA strives towards being as open as possible about how it works and how it comes to its decisions.
- EMA publishes **clear and impartial information** about medicines and their approved uses. This includes transparency of agenda and minutes of committees, public versions of scientific assessment reports and summaries written in lay language.
- The public has the right to request information and documents from EMA in accordance with its rules on access to documents and on access to information.
- Since October 2016, EMA publishes **clinical data** submitted by pharmaceutical companies to support their regulatory applications for human medicines under the centralised procedure.

Any questions?

Further information

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The EU Marketing Authorisation

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18 September 2017

Presented by Rocio Gonzalo Ruiz
Procedure Management Department

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The Centralized Procedure
Pre-Submission
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Marketing authorisation

EU law requires all medicinal products to obtain a Marketing Authorisation (MA) before they can be placed on the market.

- **Directive 2001/83/EC** - The core legislation governing the regulation of drugs in EU
- **National Law**, implementing Directive 2001/83/EC at national level
- **Regulation (EC) No 726/2004** – sets out the centralised procedure

Choice of the authorisation route

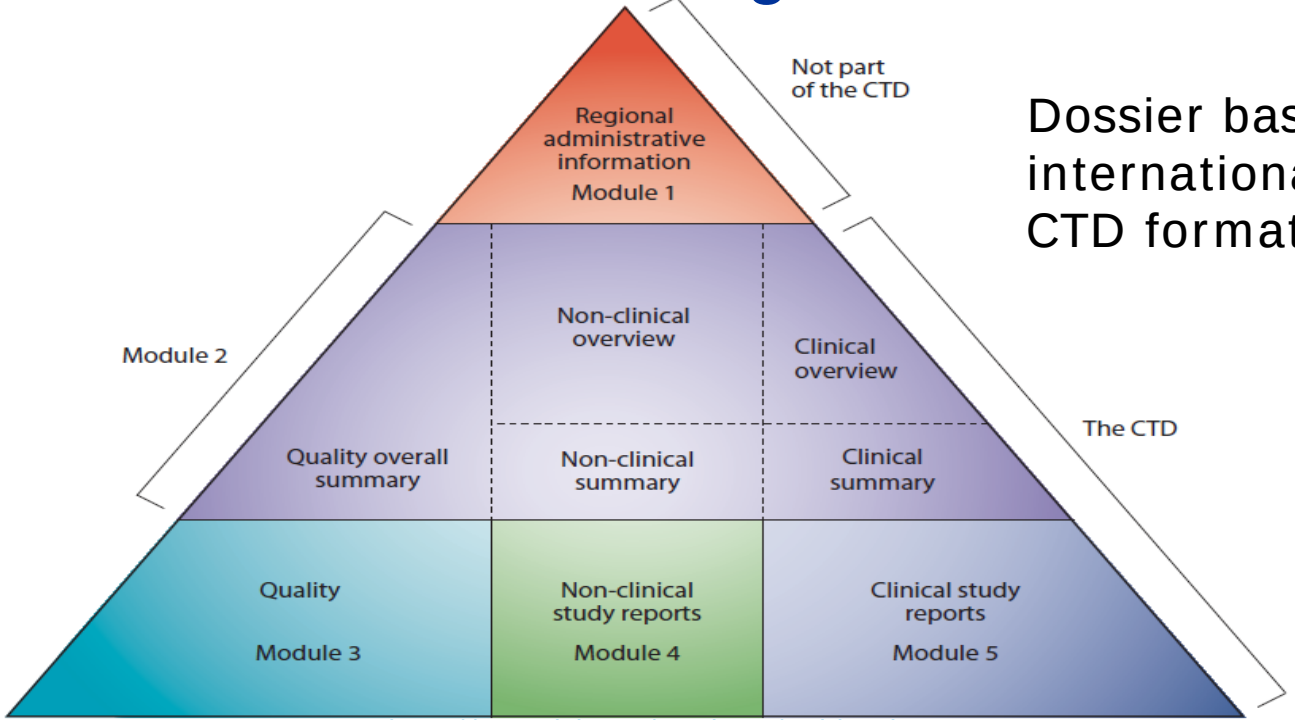
Some products can now be authorised only via centralised procedure (“**mandatory** CP scope”)

For some the applicant can choose either centralised procedure or national/ MRP/ DCP procedure (“**optional** CP scope”)

Some products are excluded from centralised procedure (**outside** of any CP scope)

Eligibility for centralised procedure has to be confirmed in advance of submission of the MA application

Requirements for Marketing Authorisation



Dossier based on an internationally agreed CTD format.

http://www.ich.org/products/ctd.html

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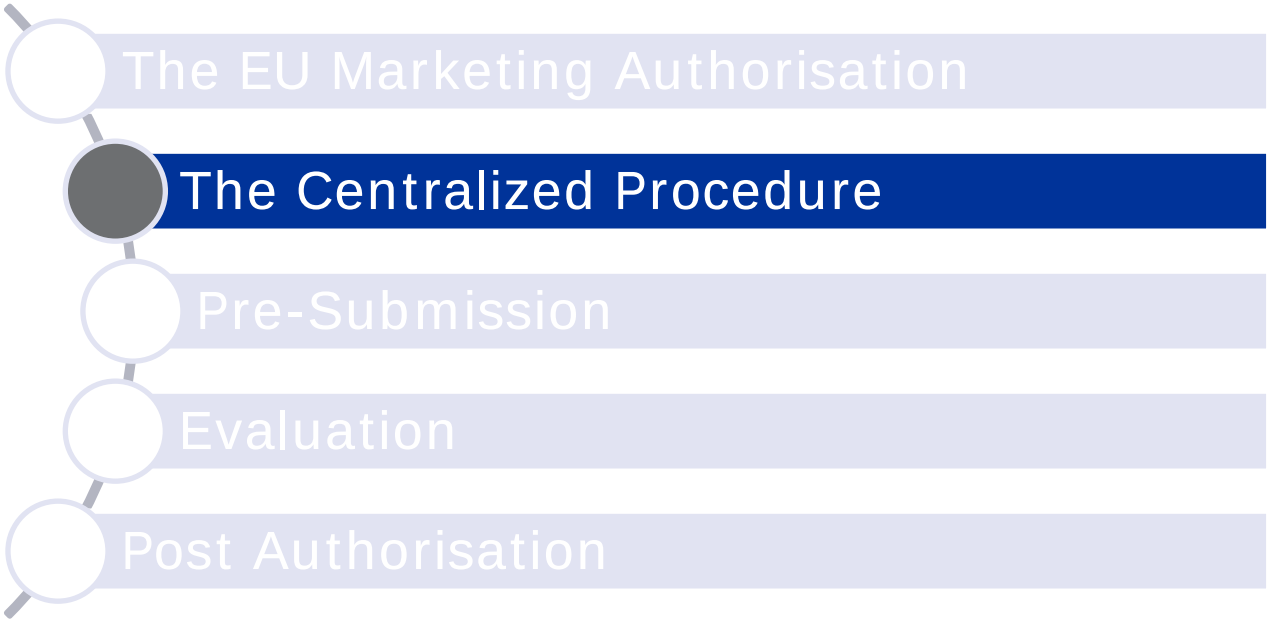
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A system based on Trust & Reliance

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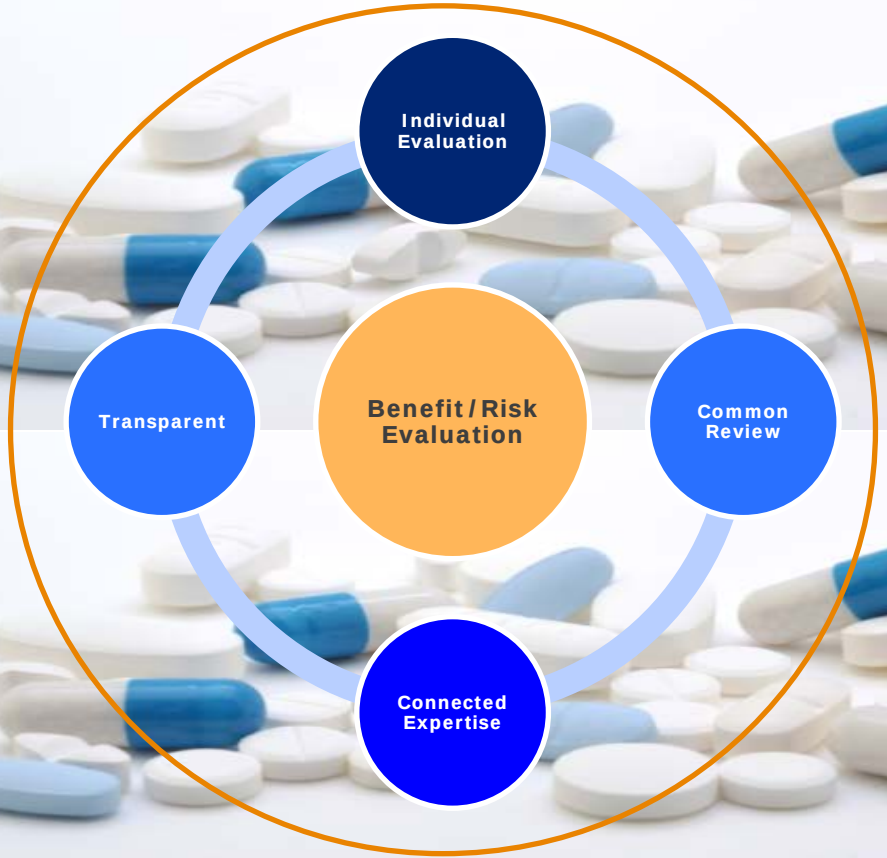

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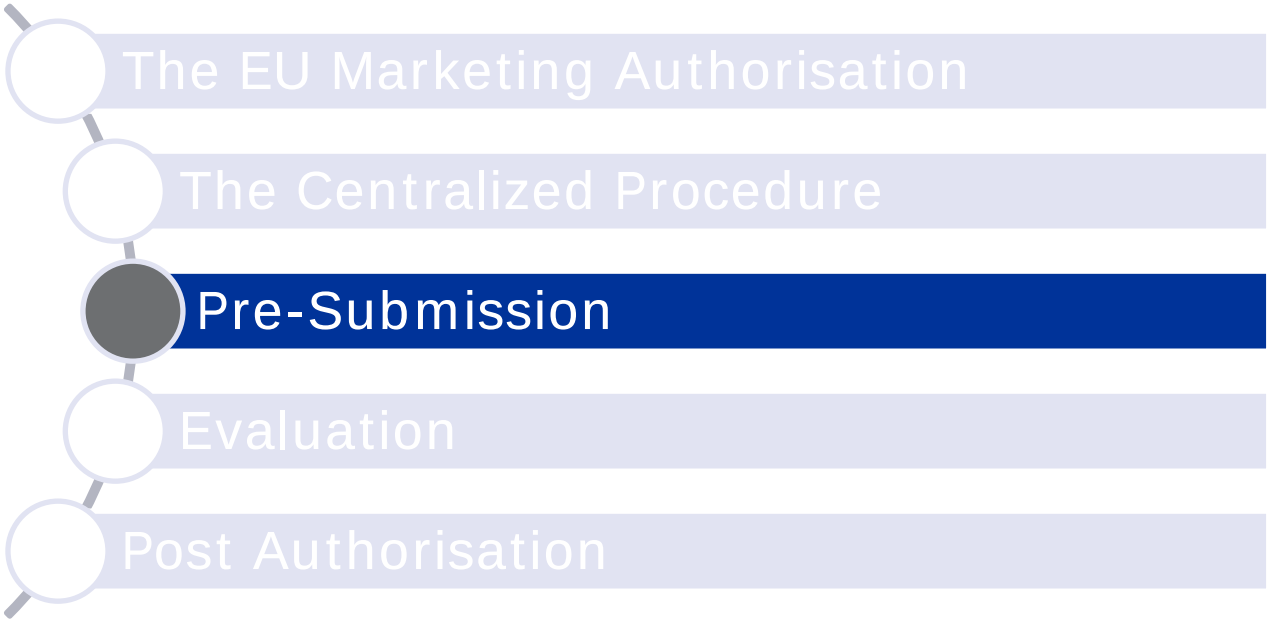
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Pre-submission for centralised procedure

Request for accelerated assessment

Presubmission meeting

Letter of intent to submit

Appointment of Rapporteurs

Request Eligibility for Centralised Procedure

Request Invented name review

ATMP certification

CHMP Opinion on compassionate use (triggered by MSs)

Scientific Advice / protocol assistance

Pipeline information

SME designation

Paediatric requirements

Innovation task force

Orphan designation

ATMP classification

Mandatory steps

NEW

Priority medicines (PRIME) scheme launched in March 2016

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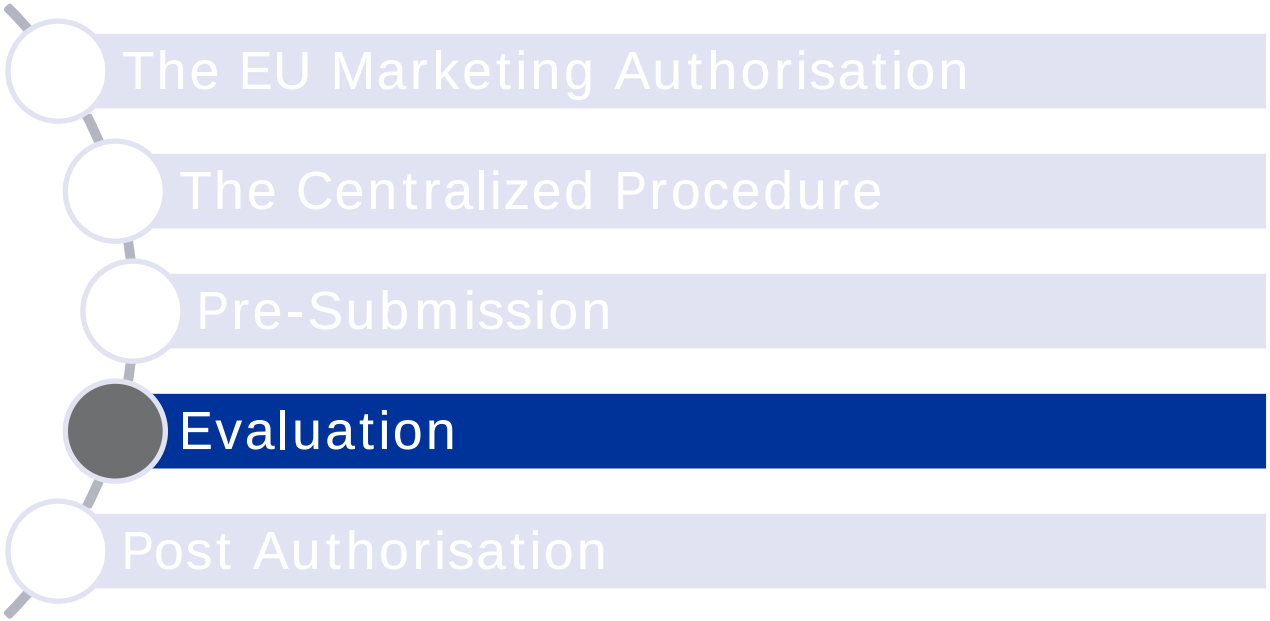
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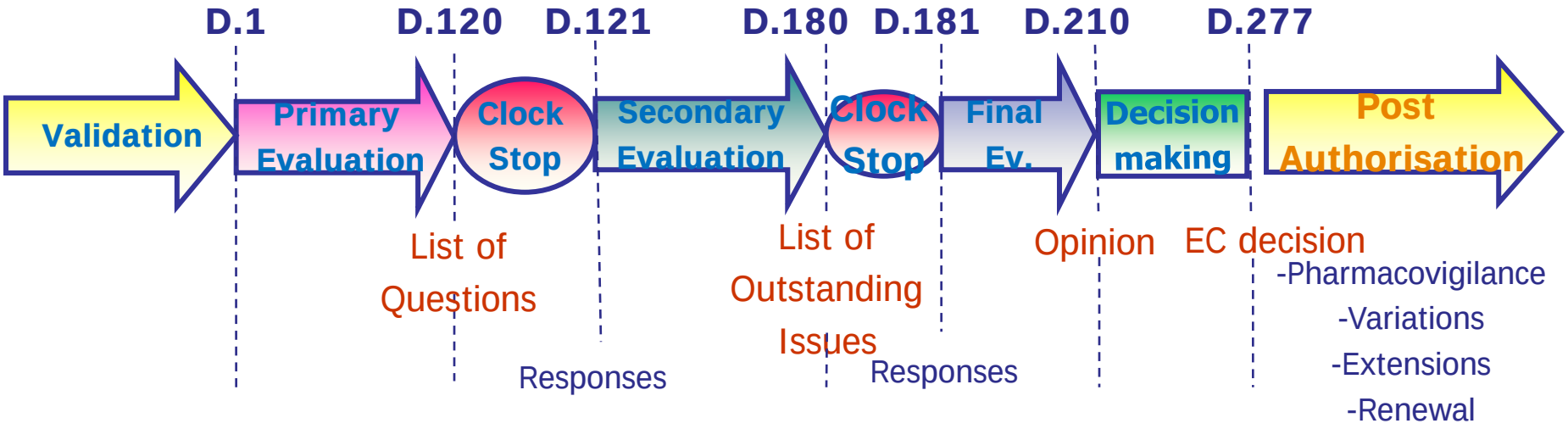
Assessment process in centralised procedure

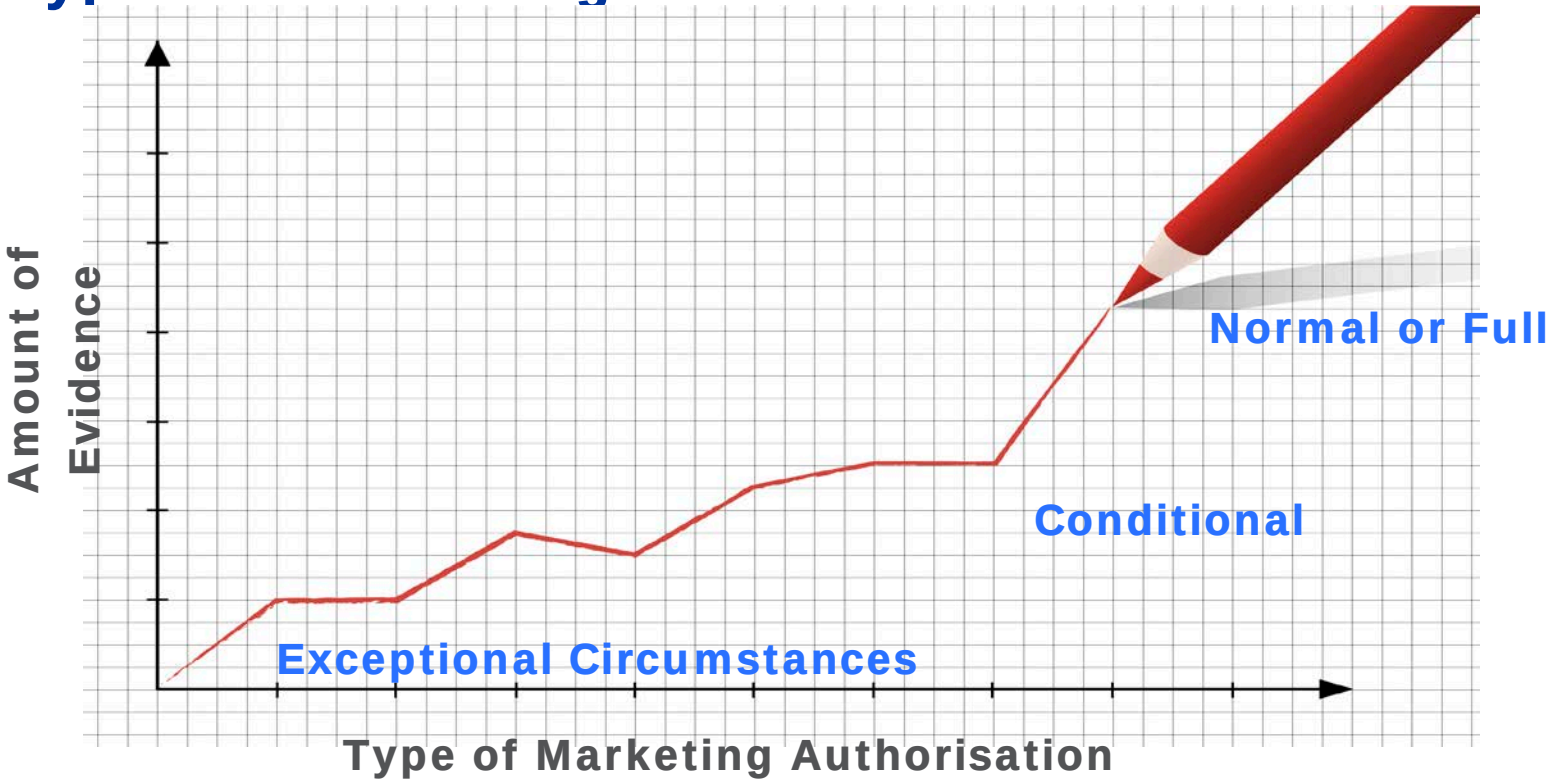


The system is collaborative, connected, and transparent

Adoption of CHMP Opinion

- The CHMP assessment and Opinion:
  - ➢based on scientific criteria
  - ➢determine whether or not the products meet the **quality**, **safety** and **efficacy** requirements
  - ➢ensure that medicinal products have a **positive risk-benefit balance** in favour of patients/users
- CHMP Opinion adopted by **consensus or majority vote**
- In case of majority vote – **divergent opinions** of minority included in the final documents.

Types of marketing authorisations



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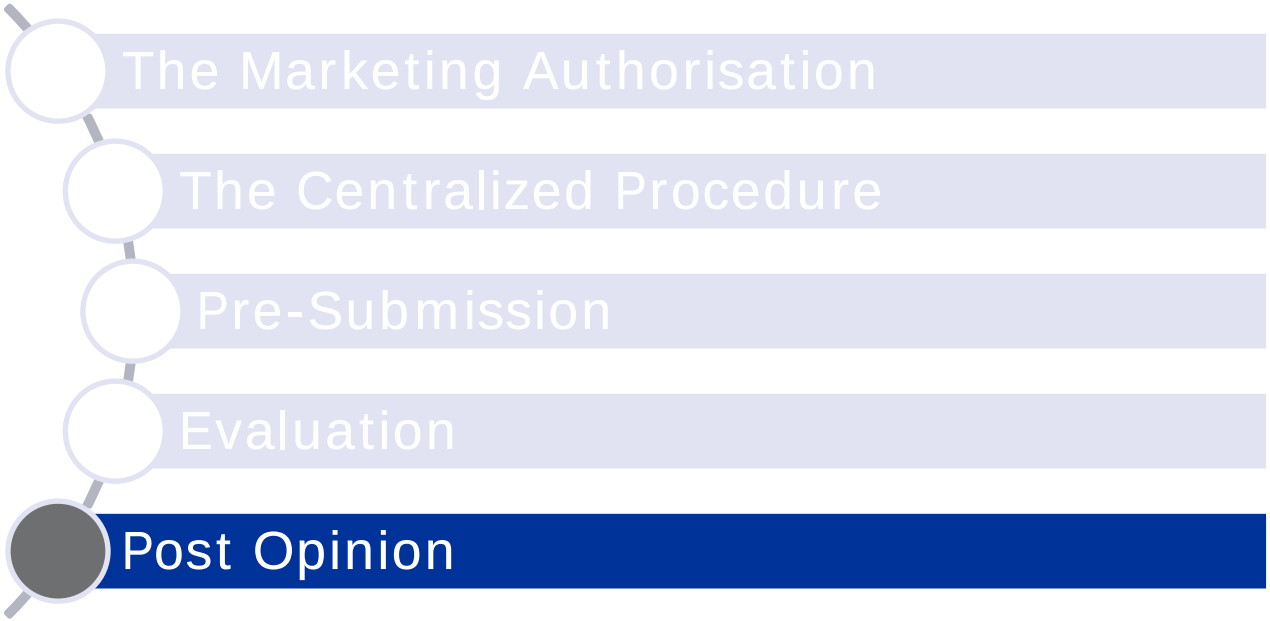
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Centralised procedure (post-opinion)

- European Commission (EC) prepares **draft decision**
- **Standing Committee** on Medicinal Products for Human Use (representatives from Member States) gives Opinion on the draft decision
- EC **adopts the decision** on granting (or refusing) Marketing Authorisation, which takes effect from the data of notification
- Outcome is **published** by EC and EMA (including assessment reports and clinical data

The outcome of the decision is published in a transparent way!

Any questions?

Further information

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Lifecycle Product Management

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Presented by Helena Matos
Procedure Management Department

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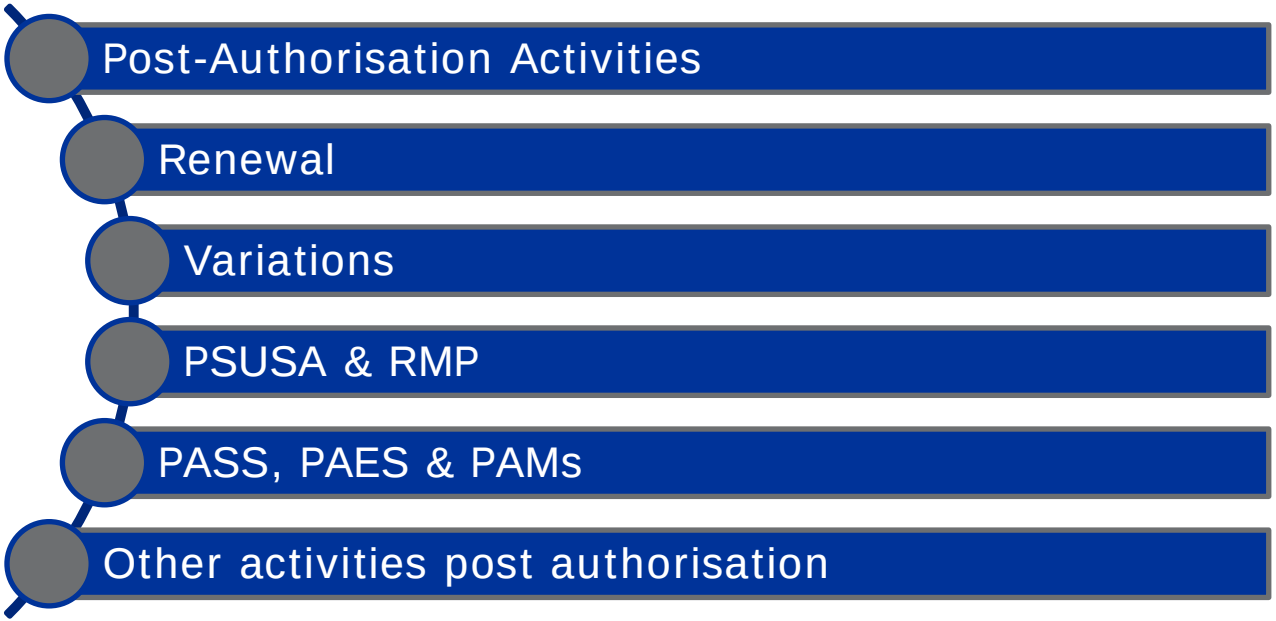
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Renewal
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Other activities post authorisation

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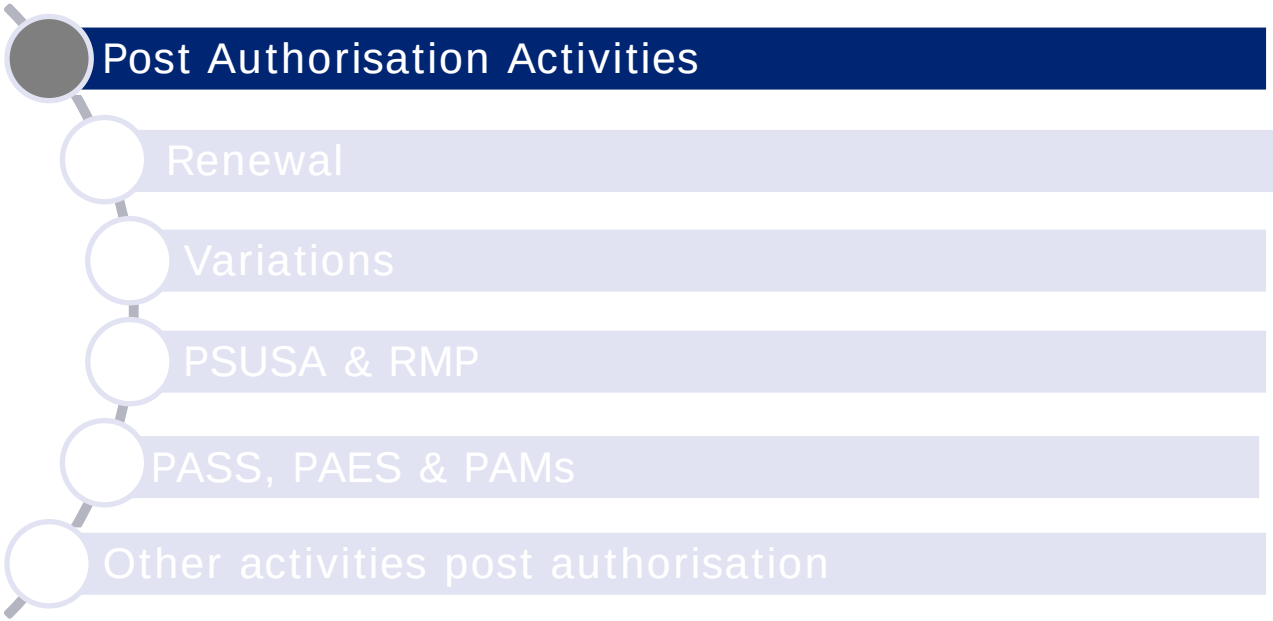
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EU law requires the holder of the marketing authorisation (MA) to take account of scientific and technical progress and to keep the MA up to date with regards to its Quality, Safety and Efficacy

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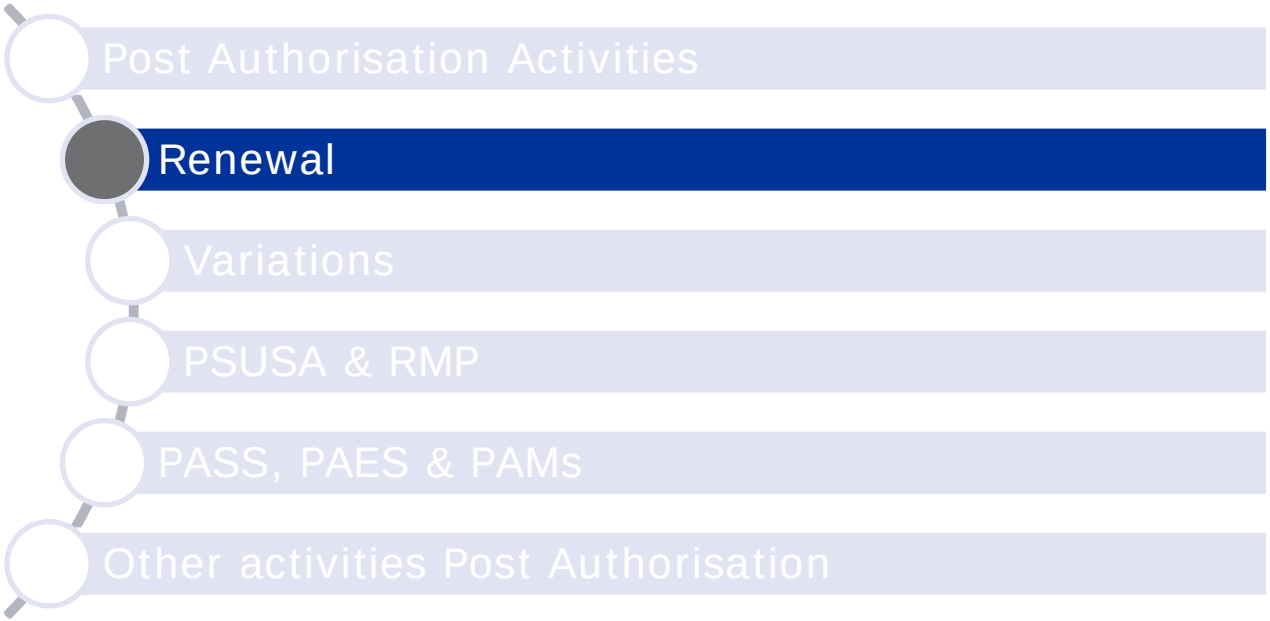
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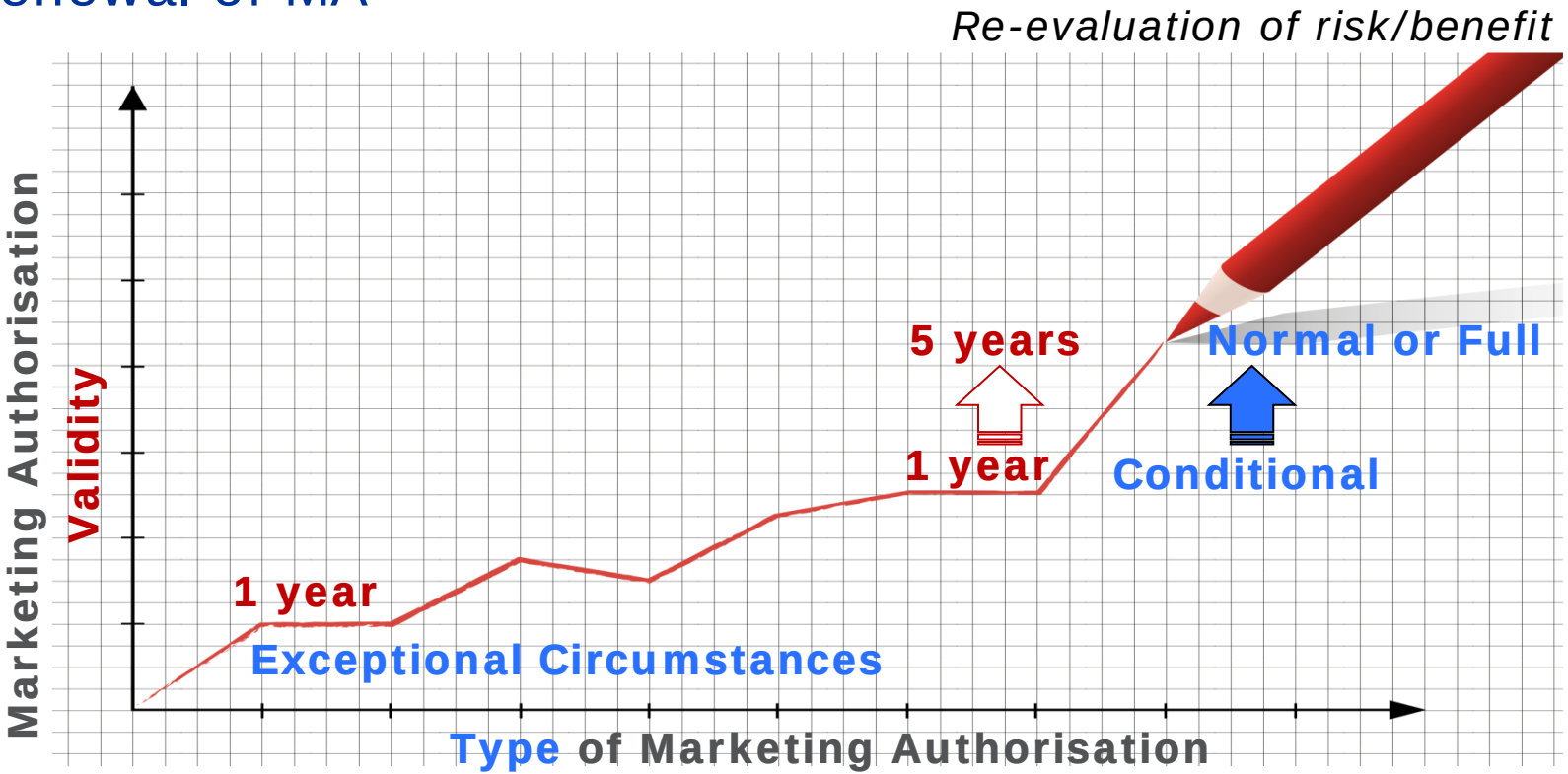
Renewal of MA



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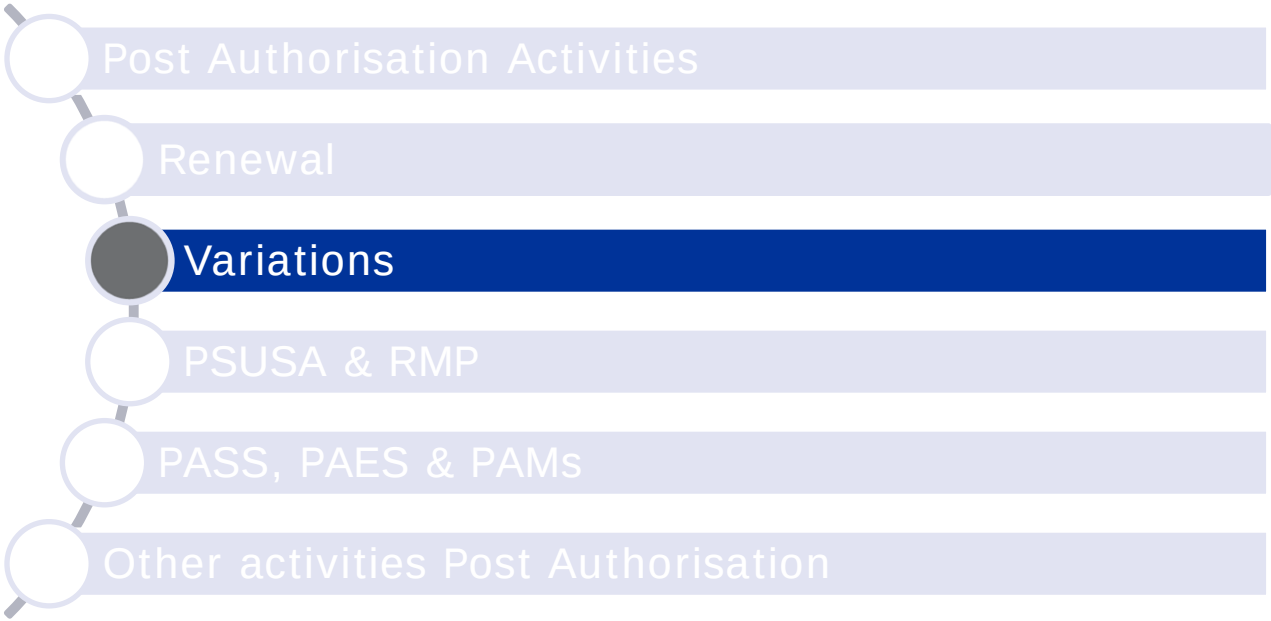
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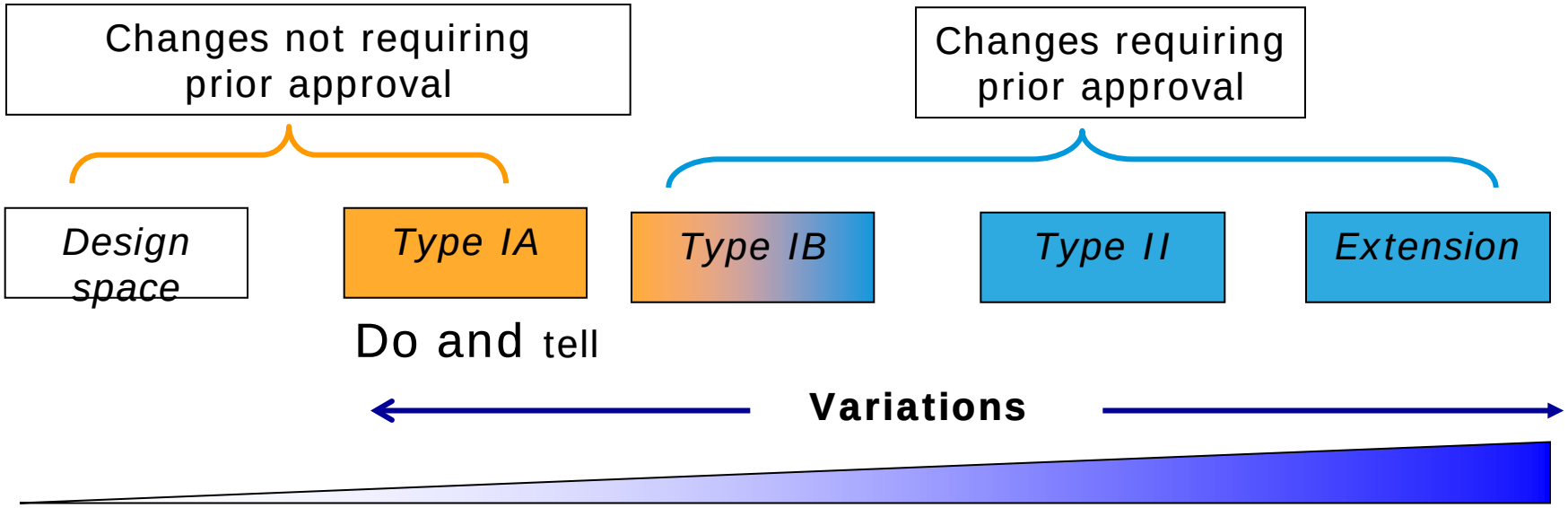
Variations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Changes requiring prior approval
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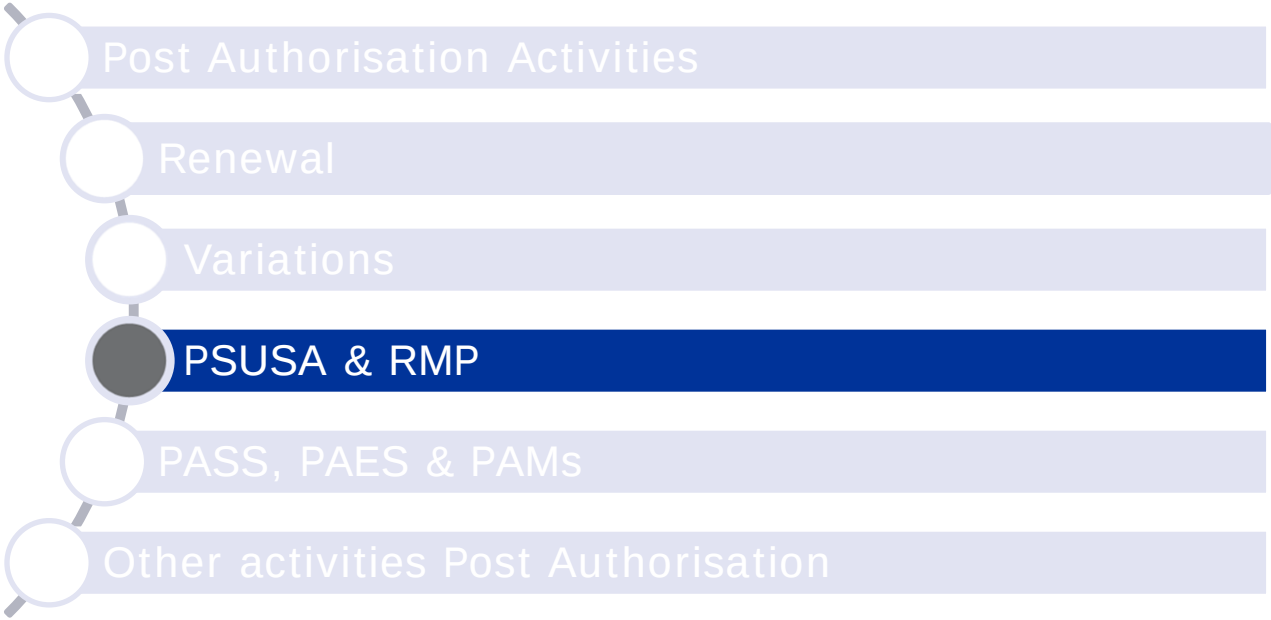
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Period Safety Update Reports (PSURs)

Periodic benefit risk ***evaluation***

Cumulative safety data

Risk Management Plan (RMPs)

- Prospective planning based on the knowledge on the product
- Risk minimisation measures
- Ensuring effectiveness of RMM

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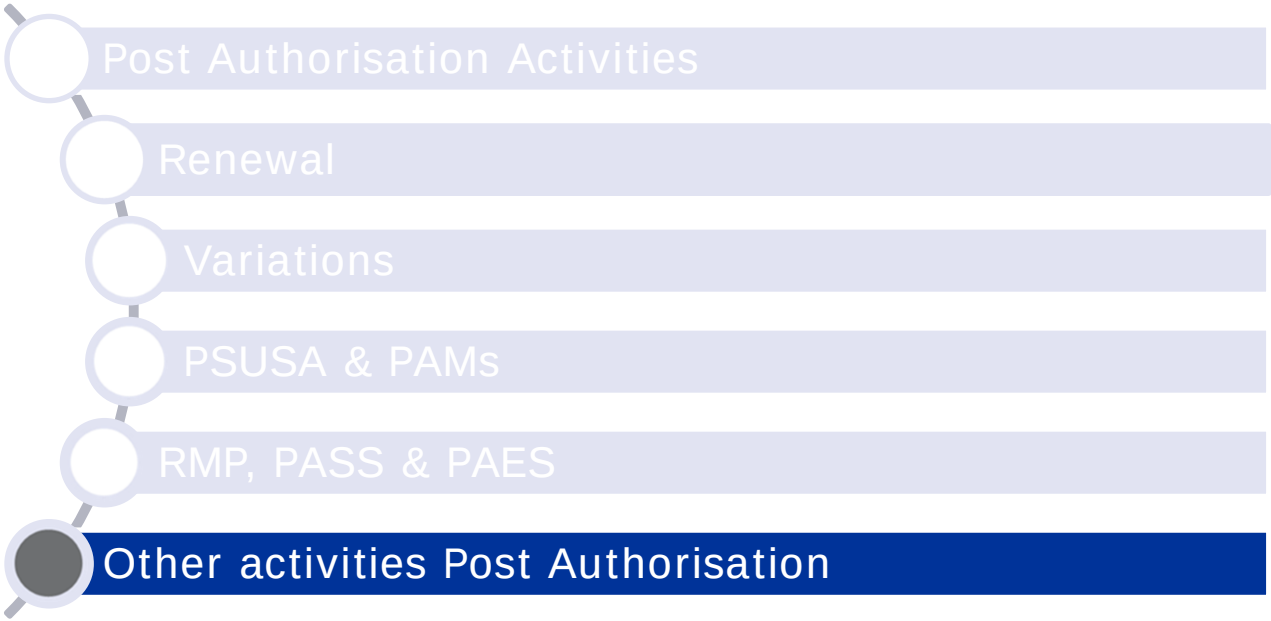
Post-authorisation studies (PASS / PAES) & Post Authorisation Measures (PAMs)

- Regulators can require studies to be conducted at first authorisation / post-authorisation
- Study is a condition of the authorisation and is legally binding
- Protocol and final study results are submitted to the EMA (e.g. PAM)

Contents


Post Authorisation Activities
Renewal
Variations
PSUSA & PAMs
RMP, PASS & PAES
Other activities Post Authorisation

Other activities Post Authorisation

Referrals

- Triggered by issues on Q, S or E

- EU assessment of the impact on the benefit risk

- Harmonised outcome across the EU

Any questions?

Further information

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