Challenges in the development and registration of orphan drugs: a Regulator Perspective

Presenter:

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Disclaimer

The views presented hereafter are those of the author and should not be interpreted as having been made on behalf of the EMA, the COMP, any of the other EMA scientific committees, nor of the FAMHP.

The Orphan Regulation

- Regulation (EC) No 141/2000 (⚕ The Orphan Regulation ⚕)
- Medicinal products for human use only
  - ➢ Diagnosis, prevention or treatment
- At any time prior to Marketing Authorisation Application (MAA)
  - ➢ Free of charge
- Accessible for commercial, academic or individual entities
  - ➢ Established in EEA

The Orphan Designation

Intended for diagnosis, prevention or treatment

(a) Condition: Life-threatening or chronically debilitating

Prevalence: Affecting ≤ 5 in 10,000 persons in the EU

OR

Condition: Life-threatening, seriously debilitating or serious and chronic

Viability: No sufficient return on investment possible without incentives

AND

(b) No satisfactory method

OR

Significant benefit over existing methods

The Orphan Designation

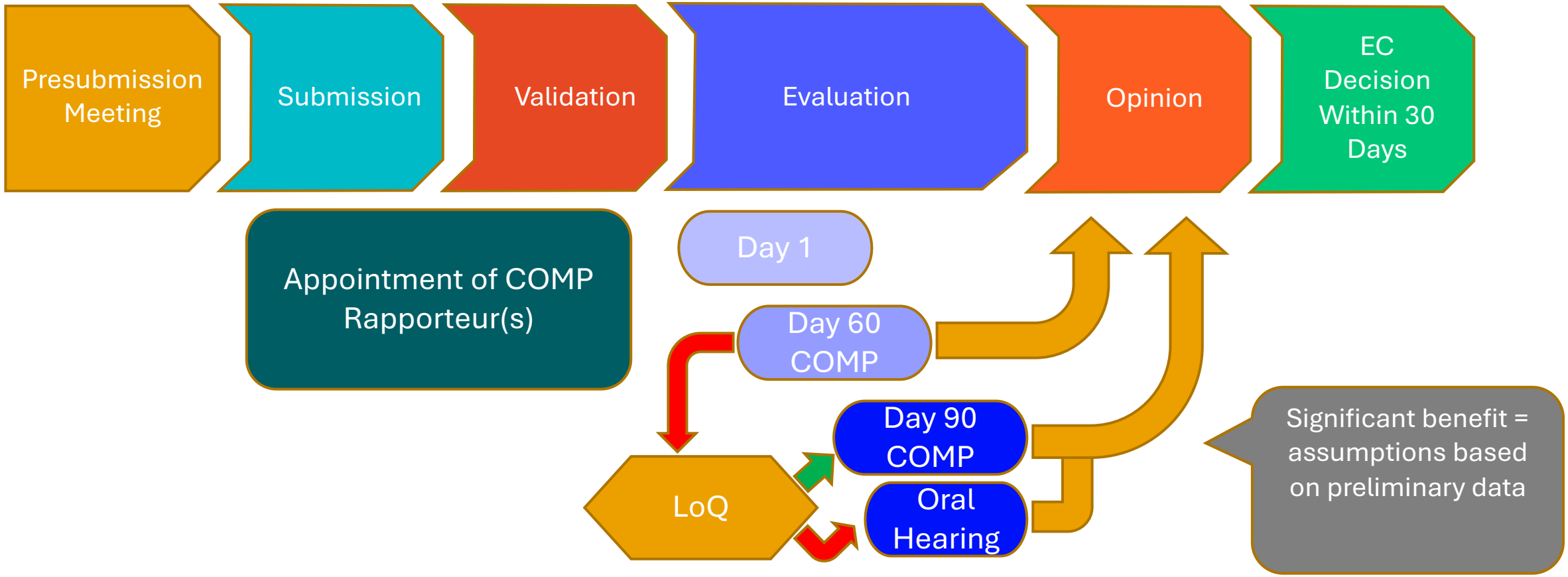
- Orphan Condition
  - ➢ Defines the Orphan Indication (OI)
  - ➢ Orphan indication ≠ Therapeutic Indication (TI)
    - TI is granted at time of MA
    - TI cannot be ‘wider’ than OI
  - ➢ Distinct deviation from normality
    - Subsetting only allowed in specific cases

The Orphan Designation

- Medical plausibility
- Prevalence criterion OR Return on Investment Criterion
- **Significant Benefit**
  - ➢ Relevant advantage over existing satisfactory methods
    - Efficacy
      - Safety
        - Major Contribution to Patient Care

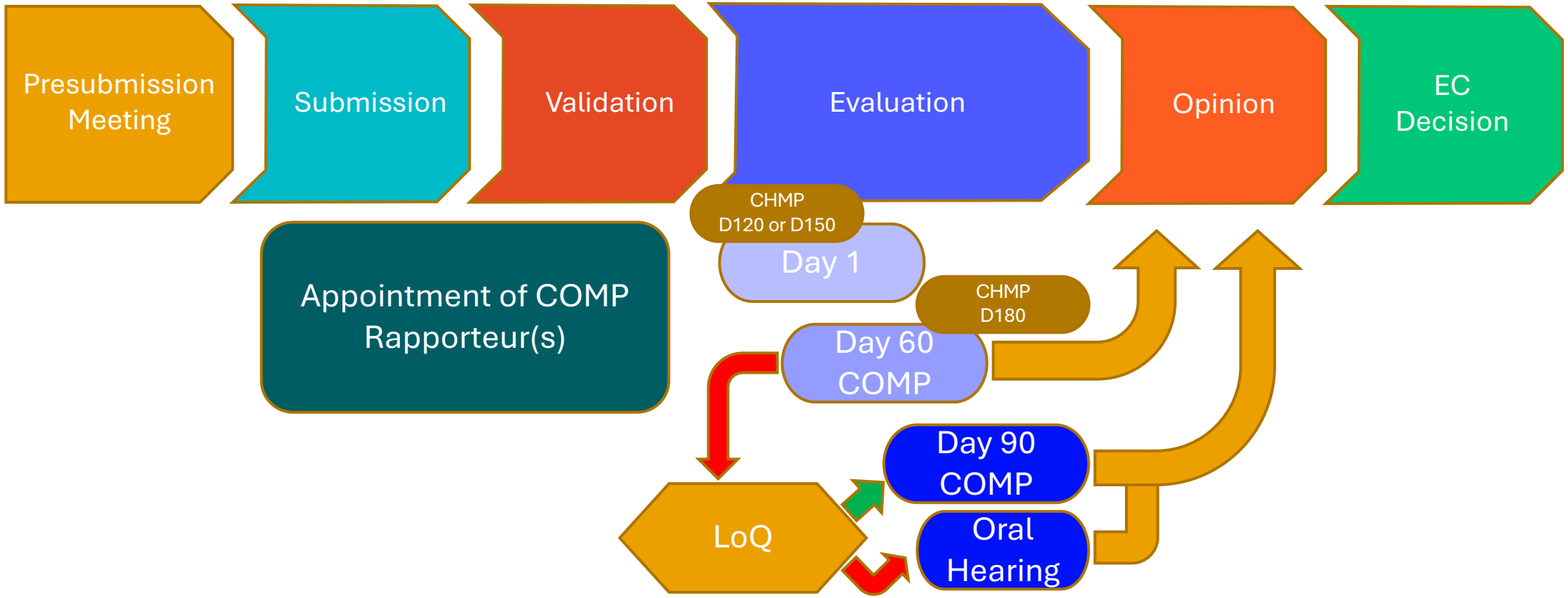
The Orphan Designation

Initial Orphan Designation



The Orphan Designation

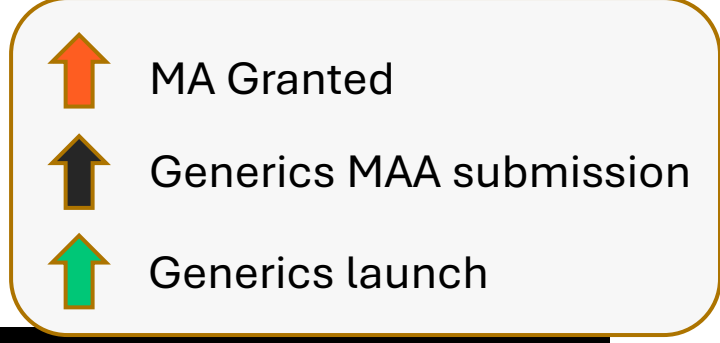
Review of OD Maintenance at MA



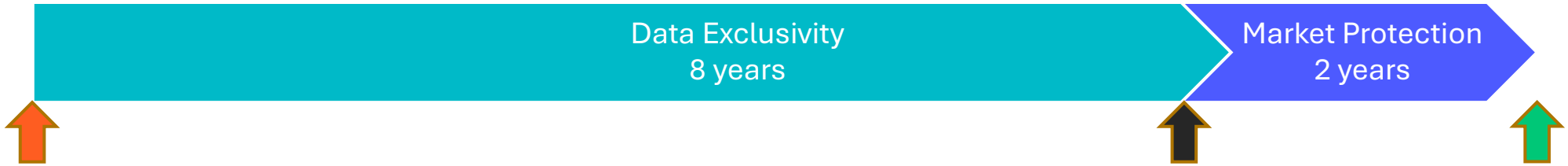
The Orphan Designation

- Multitude of incentives pre and post MAA
  - Fee reductions
  - Access to protocol assistance (Article 6)
  - Regulatory guidance for SMEs
  - Access to Centralised MA procedure (Article 7)
  - Possibility of Conditional MA
  - 10 Year Market Exclusivity (ME) (Article 8)
  - Additional national incentives (EC Inventory, Article 9)

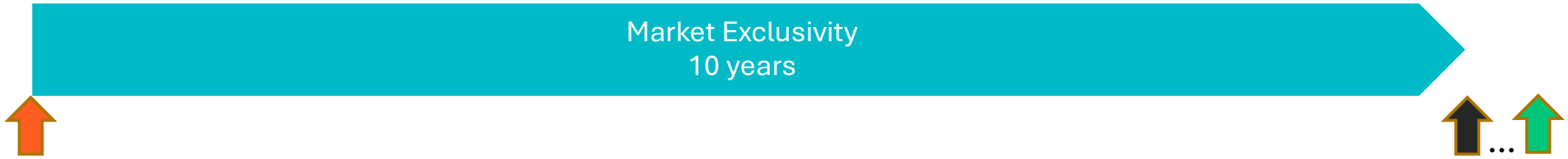
The Orphan Designation



Regular MA



Orphan Market Exclusivity



Orphan Market Exclusivity + PIP compliance

The Orphan Designation

- Failure to achieve OD does not mean a prodcut cannot come to the market
  - ➢ Only loss = orphan incentives
- COMP has no legal mandate to take into consideration pricing issues
  - ➢ Pricing is solely the remit of Member States' HTAs

Committee for Orphan Medicinal Products (COMP)

- Inaugurated in April 2000 (EC 141/2000, Article 4)
- Monthly meeting, 11 times per year (August excluded)
- Issues opinions, not final decisions
  - ➢ Final decision = European Commission
- 27 EU delegates, 2 EEA-EFTA delegates, 3 patient experts, 3 coopted members, 1EC Representative, 1 EURORDIS observer

New Pharma Legislation = New Frontiers

- Commitees as they exist will cease to be
  - ➢ Except CHMP, CVMP and PRAC
  - ➢ Replaced by expertise based working parties/groups
- Reduction in Orphan incentives
  - ➢ Regulatory sandbox
- Orphan = rare

Recent challenges in designations

- ATMPs
  - N of 1 trials
  - In silico development
- Significant benefit claims in crowded areas
  - MAIC, unanchored indirect comparisons, etcetera
- Complex genetic spectrum diseases
- Interpretation of the SmpC in context of establishing satisfactory methods

Patient empowerment

- COMP = 1st committee with patient experts as full members
  - Rapporteurship
  - Full voting rights
- Huge positive difference in the discussions
  - Every patients is the world most eminent expert when it comes to his/her/their needs
- Incorporating patient-led suggestions enriches applications
  - Active, not passive input

New technology

- Use of LLMs (ex. CollaboRARE)
  - ➢ Major contribution to patient care discussion
    - Automated ranking of preference and experience data
    - Based on publicly available data from websites, blogs, fora, etc.
    - Validated by patient organisations
  - ➢ Endpoint validation
  - ➢ Regulatory data and guideline retrieval
    - Currently Over 6000 documents on EMA website