Regulatory challenges in rare cancers drugs development

Kyriaki Tzogani
Scientific Administrator
Oncology, Haematology and Diagnostics Office

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Orphan Regulation in the EU

- **Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products of 16 December 1999**
  - Criteria for designation
  - Committee (COMP) - Procedure
  - Incentives (market exclusivity)
- **Commission Regulation (EC) No 847/2000 of 27 April 2000**
  - criteria for designation of a medicinal product as an orphan medicinal product
  - definitions of the concepts 'similar medicinal product' and 'clinical superiority'
- **Commission notice on the application of Articles 3, 5 and 7 of Regulation (EC) No 141/2000 on orphan medicinal products**

Designation criteria

- **Rarity (prevalence)**

Medical condition affecting not more than 5 in 10,000 in the Community (around 250,000 people)

- **Seriousness**

Life –threatening or chronically debilitating

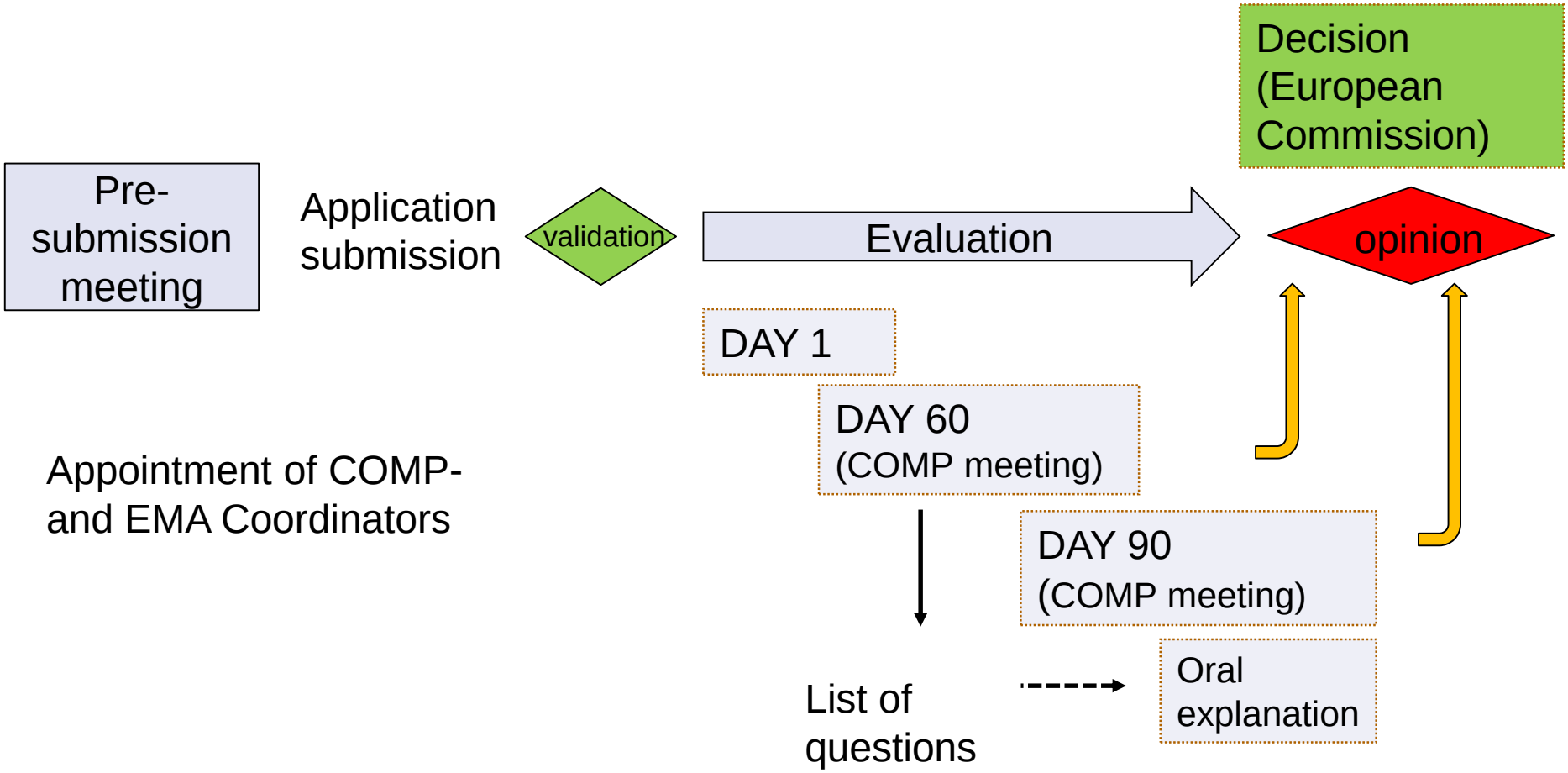
- **Alternative methods authorised**

No satisfactory methods of treatment or if existing significant benefit to be demonstrated

Committee for Orphan Medicinal Products (COMP)

- 1 Elected Chair
- 1 Vice chair (Patient Rep)
- 1 Representative per Member State (28)
- 3 Patients' Representatives appointed by European Commission
- 3 Members appointed by European Commission on proposal from Agency
- 1 Member for Norway, and 1 for Iceland

The designation process in the EU



Incentives

Protocol assistance/Scientific Advice

Market exclusivity

Fee reductions

Extended incentives for SMEs

Access to the centralised authorisation procedure

Significant benefit

Satisfactory Methods of Treatment, Diagnosis or Prevention

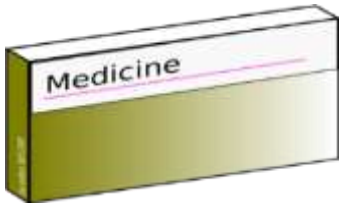
No methods

Methods unsatisfactory

No SB needed

Methods Satisfactory

Need to justify SB assumptions



Significant benefit

- Unique to the European Orphan Regulation

- Defined as:

  - **a clinically relevant advantage**

  - **a major contribution to patient care**

Clinically relevant advantage

- improved efficacy for the entire population suffering from the condition or a particular population subset or a subset that is resistant to the existing treatments

or

- a better safety profile or a better tolerability for the entire population suffering from the condition or for a particular subset

Major contribution to patient care

- ease of self-administration

- significantly improved adherence to treatment due to a change in pharmaceutical form

Theoretical examples

Pills vs. injection (but not 3 pills a day vs 1 injection per month)

Ready to inject vs need to reconstitute (sterile)

Easy to carry (e.g. not requiring storage in the fridge)

Significant benefit

Should not be based on:

- possible increased supply/availability due to shortages of existing authorised products or to existing products being authorised in only one or a limited number of Member States (except evidence of patient harm)
- a new pharmaceutical form, a new strength or a new route of administration unless it brings major contribution to patient care
- an alternative mechanism of action *per se*

Orphan Similarity

- Paragraph 3 of Article 8 of EC Regulation 141/2000 establishes the basis for Orphan Medicinal Similarity.
- Orphan Similarity occurs when a product is submitting for an indication where there is a already one or more Orphan Designated products authorised which have an active 10yr Market Exclusivity (not expired).
- Orphan Similarity involves three similarity tests:

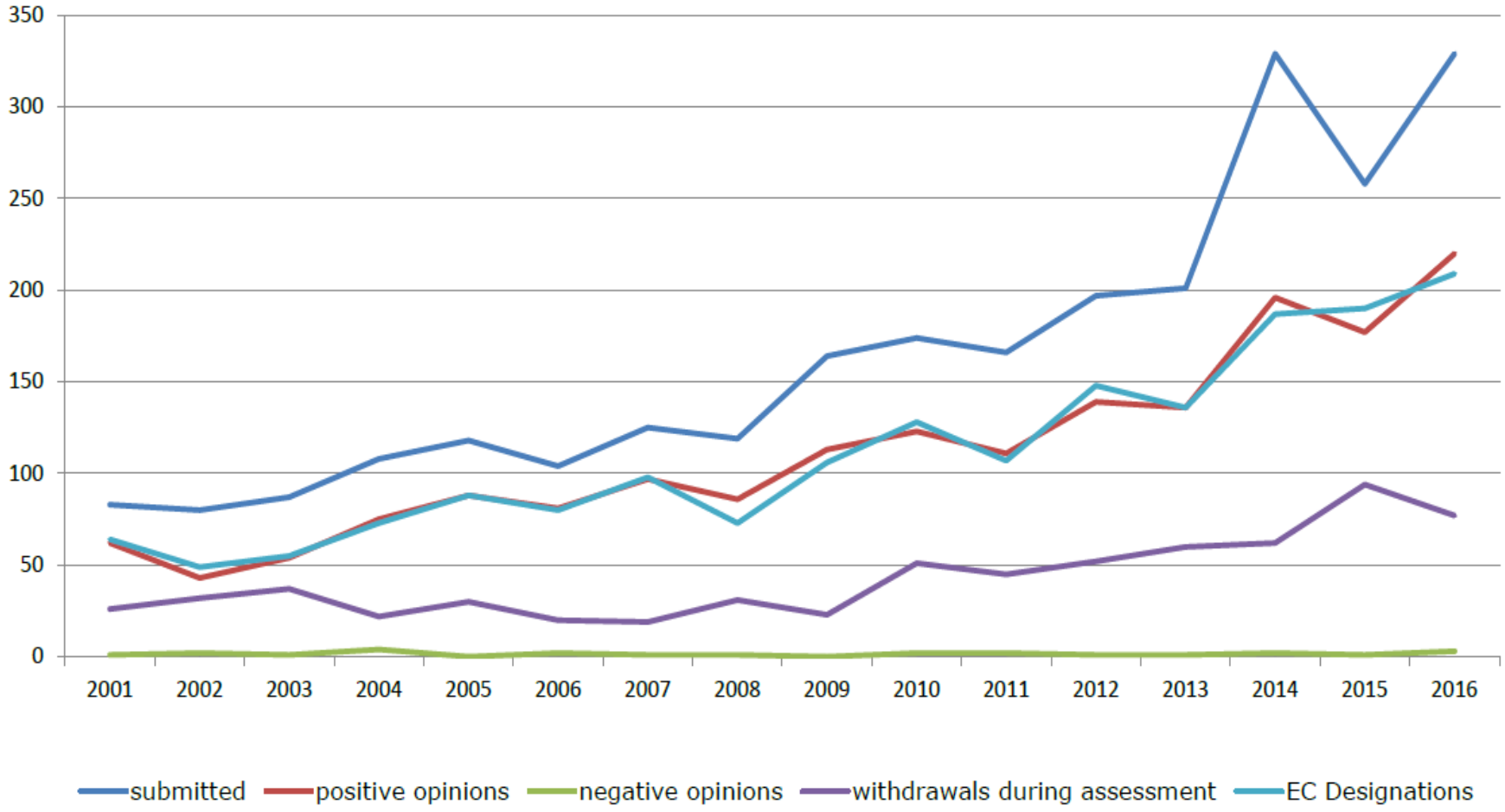
  Structure, mode of action and therapeutic indication.

Derogations to market exclusivity if Orphan Similarity applies

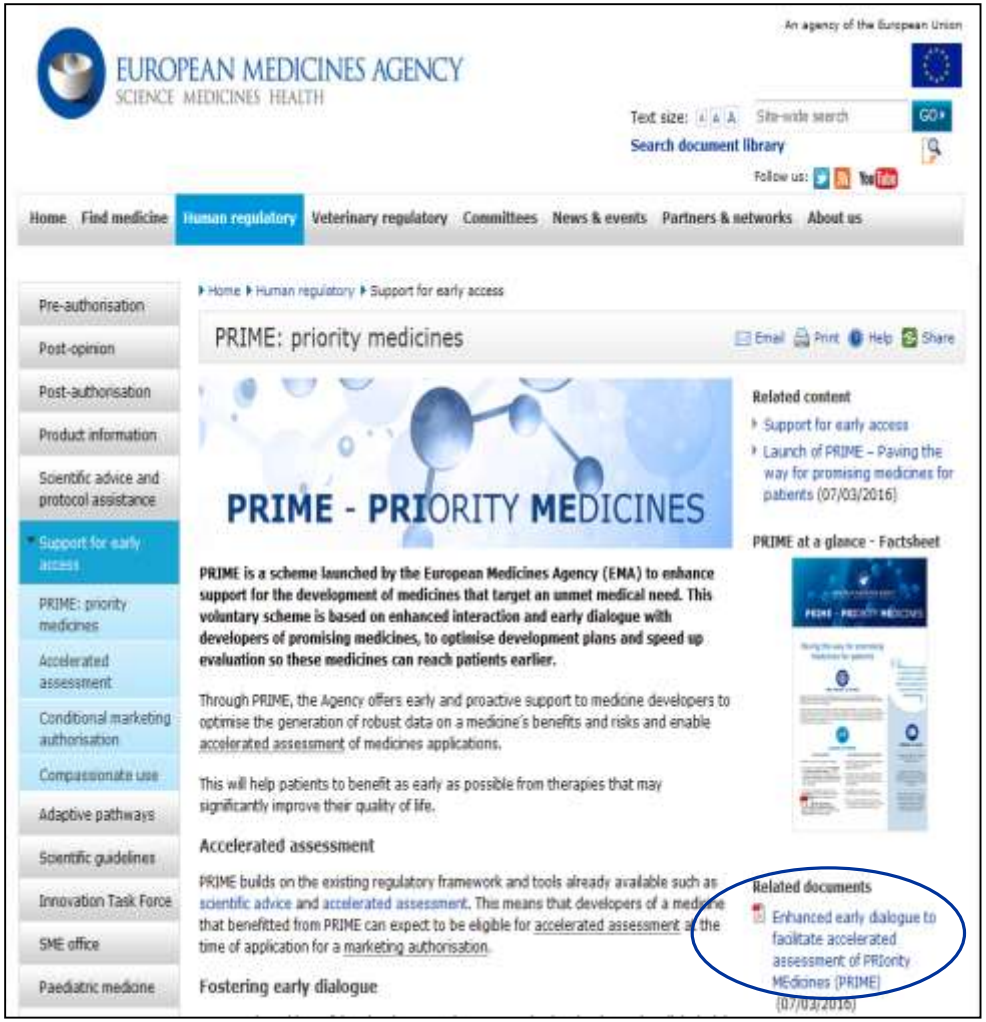
Three derogations (Art 8(2))

- First MAH's consent (agreement market sharing)
- Insufficient supply: long term and clinical consequences (presumably)
- Clinical superiority: better efficacy, better safety or exceptionally major contribution to patient care

Status of orphan applications



PRIME was launched in March 2016



Factsheet in lay language

Q&A, templates, application form for applicants

prime@ema.europa.eu

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Thank you for your attention!

Further information

Contact me at Kyriaki.Tzogani@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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