EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Orphan drug designation in the European Union

Joint EMA/FDA/MHLW-PMDA orphan medicinal product workshop
10 March 2014

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Head of orphan medicines (ad interim)

Outline

Overview orphan designation and criteria

- Definition of a distinct medical entity
- Significant benefit

Procedure of designation and the review of the ODD criteria at the time of MAA

Experience so far

- Orphan designation
- Marketing authorisation

Main characteristics orphan designation

Applications for treatment, prevention or diagnosis of rare diseases

Procedure free of charge

Designation can be requested at any stage of development before the application for MAA is made

Sponsor can be either company or individual

- Established in the EEA (EU, Ice, Liech, Nor)

European Commission Decision gives access to incentives such as protocol assistance

Designated products are entered into the Community Register of OMPs by the EC

Committee for Orphan Medicinal Products (COMP)

- 1 elected Chair (Prof Bruno Sepodes)
- 1 Representative per Member State
- 3 Patients' Representatives appointed by Eur. Commission
- 3 Members appointed by Eur. Commission on proposal from Agency
- 1 Member for Norway and 1 for Iceland

TOTAL: 33 members + 2 non voting

COMP responsabilities

- Give opinions on designation
- Advise Commission on establishment and development of a policy on orphan medicinal products
- Assist Commission in international liaison
- Assist on Commission in drawing guidelines
- Contribute to Protocol Assistance (esp Significant Benefit)

Designation criteria

RARITY (prevalence) / RETURN OF INVESTMENT (Art 3.1 (a) of 141/2000)

- Medical condition affecting not more than 5 in 10,000 in the Community (around 250,000 people)
- Without incentives it is unlikely that the marketing of the product would generate sufficient return to justify the necessary investment

SERIOUSNESS

- Life –threatening or chronically debilitating

ALTERNATIVE METHODS AUTHORISED (Art 3.1(b)of 141/2000)

- If satisfactory method exist the sponsor should establish that the product will be of significant benefit

EXCLUSIVE for EU

Application package

Cover letter

Application form

Scientific sections A-E of the application

Proof of establishment of the sponsor in the EU

Translations of the name of the product and the proposed orphan indication into the official languages of the European Union, plus Icelandic and Norwegian

Bibliography

If applicable, letter of authorisation from the sponsor for the person/company acting on their behalf during the procedure

How to apply for orphan designation

This page provides information for sponsors on how to apply for orphan designation for a medicine.

Notification of intention to submit

Sponsors should notify the EMA of their **intention** to submit an application as early as possible, and at the latest two months prior to the planned submission date. This notification should be sent by e-mail orphandrugs@ema.europa.eu and should include:

- name of the active substance;
- proposed orphan indication (i.e. treatment, prevention or diagnosis of a rare disease);
- name and address of the sponsor;
- planned submission date for the designation application and the proposed date for a pre-submission meeting (if required);
- Unique Product Identifier (UPI) number. If you already have a UPI number please quote it in all your correspondence. Otherwise, the number will be assigned automatically when we receive your intent to file and communicated to you by e-mail. However, the sponsor can apply for an UPI number at any stage of product by completing the UPI registration form below and sending it to upiregistration@ema.europa.eu.
  - Unique Product Identifier registration form

Presubmission meetings

The Agency strongly encourages sponsors to request a **presubmission meeting** with the

Related information

- Orphan designation
- Medicines for rare disea
  background information

Contact point:

orphandrugs@ema.europ

Guidance and forms
Herbal products
Referral procedures
Article 58 applications
Compassionate use
Pharmacovigilance
Data submission on authorised medicines
Advanced therapies
Clinical trials
Inspections
Falsified medicines
Quality by design
Product defects and recalls
Parallel distribution
Medicine shortages
Antimicrobial resistance
Pandemic influenza

filing. Presubmission meetings for orphan designation are free of charge.

Presubmission meetings are useful since the evaluation process has a fixed duration of 90 days and cannot be lengthened to accommodate for the lack of data or other omissions in the application. Experience has shown that they have a positive impact on the success rate of the applications.

Application procedure

Sponsors should use the forms below to apply for orphan designation:

- Application form for orphan-medicinal-product designation
- Common European Medicines Agency / Food and Drug Administration (FDA) application form or application form for orphan medicinal product designation
- Template for sections A to E for the scientific part of the application for orphan designation
- Translations required with the submission of an application for orphan medicinal product designation

Refer to these documents for assistance completing these forms:

- Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another, 9 July 2007
- Points to consider on the calculation and reporting of the prevalence of a condition for orphan designation
- Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation
- Data providers and sources to identify existing authorised medicinal products in the European Union and European Economic Area

In particular, when completing section A.3.2 'Plausibility of the orphan condition; rationale for use of the medicinal product', sponsors should clearly identify studies with the substance in a relevant model(s) of the condition and, if possible, preliminary clinical data in patients with the condition.

Each application is assigned two coordinators:

- one member of the Committee for Orphan Medicinal Products (COMP);

Medical condition

EC Guideline on the format and content of applications as OMPs (ENTR/6283/00)

- Any deviation(s) from the normal structure or function of the body, as manifested by a characteristic set of signs and symptoms (typically a recognised distinct disease or a syndrome)
- Distinct: pathophysiology, histology, clinical presentation, plausible to develop
- Different degrees of severity- stages not acceptable
- Subset of patients where positive B/R is expected generally neither sufficient to define a distinct condition
- “Special considerations”- sub-setting/intersection of 2 conditions/need for a particular treatment modality

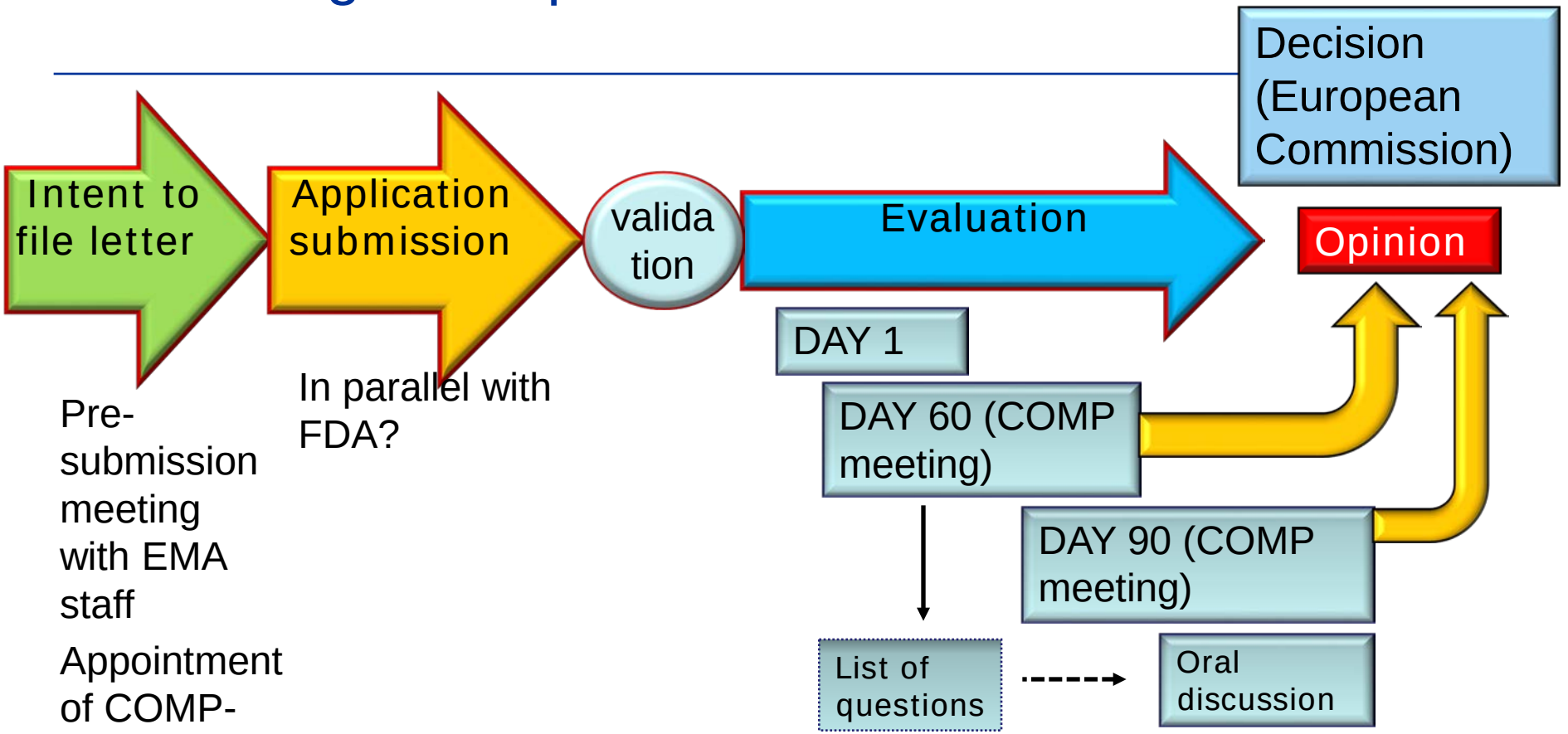
Significant benefit (Exclusive for Europe)

Significant benefit: “A clinically relevant advantage or a major contribution to patient care”

Based on **assumptions** at the time of orphan designation

- Significant benefit over “satisfactory methods”
- COMP to assess whether or not assumptions are supported by available data/evidence supplied by applicant
- Sign benefit to be **confirmed** at the time of marketing authorisation to maintain orphan status. Data to demonstrate the SB.
- Recommendation document on data for SB and plausibility

The designation process in the EU



Review of the orphan criteria at the time of MAA

At the time of submission for MAA, the sponsor is requested to submit a report on the maintenance of ODD criteria.

Guidance on the submission of this report in the pre-submission mtg for MAA.

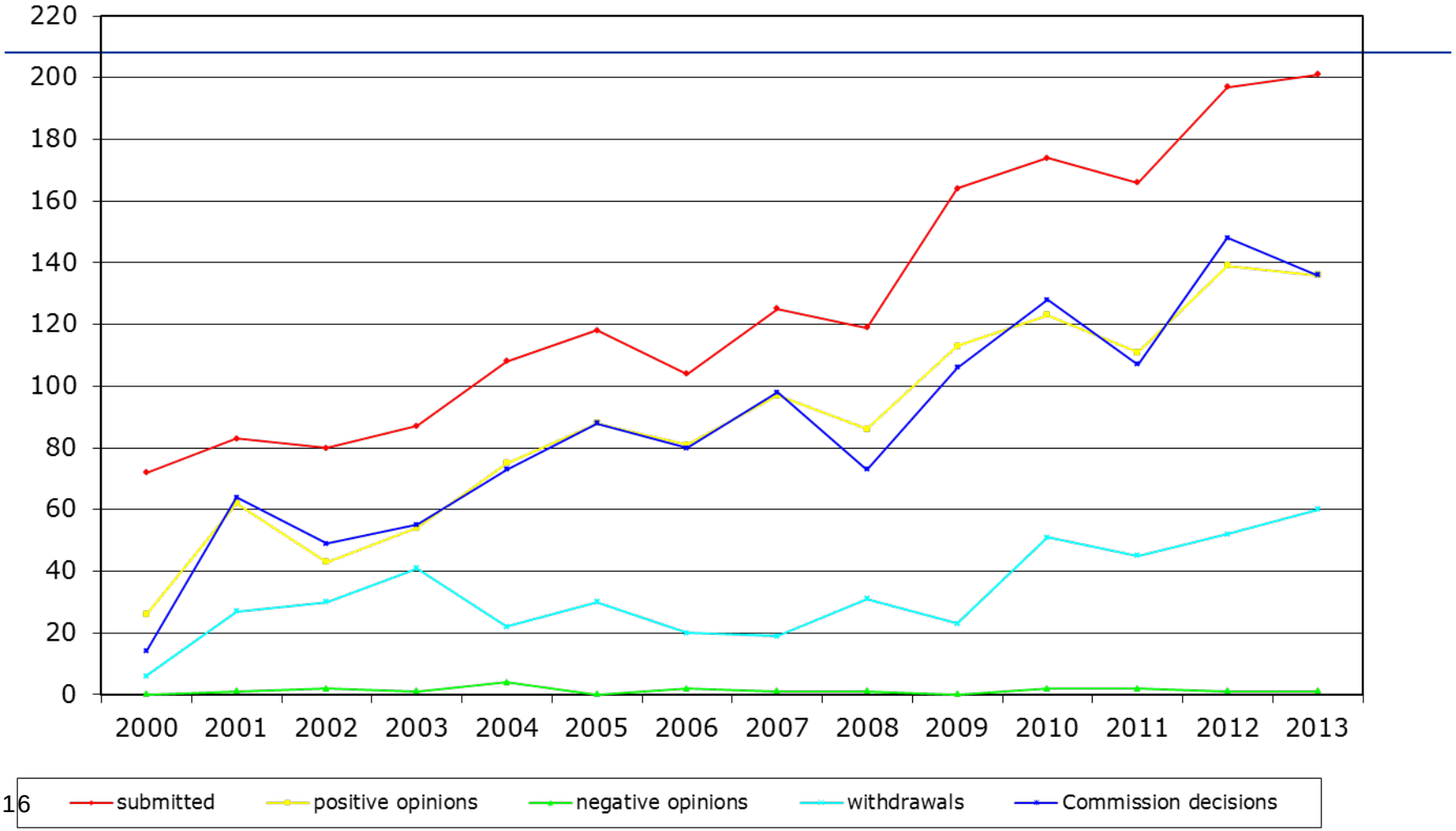
The COMP re-evaluates the fulfilment of the criteria in parallel to the MA assessment, if doubt the sponsor will be invited for an oral hearing.

The opinion by the COMP on if the product should be removed or not from the Community Register

Experience so far

- Orphan designation
- Marketing authorisation

Number and Outcome of Orphan Applications



Authorised Orphan Medicinal Products in Europe

85 marketing authorisations granted for 74 different conditions (up to Dec 2013).

The majority of the products are in the oncology therapeutic area.

Approximately 20-25 orphan MAAs expected in 2014

Conclusions

- Orphan designation is centralised in the EU
- Applications to be submitted to EMA and assessed by COMP; designations by European Commission
- Free of charge; the Sponsor needs to be established in the EU
- Significant benefit exclusive to EU: justifications to support claims (even at early stage)
- In the EU, more than 85 orphan medicinal products authorised

Acknowledgements and contact

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