EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Regulatory Perspectives ICORD

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# Declaration of Interests

Full time employee of the European Medicines Agency

No conflicting interests (no grants, shares, patents, etc.)

# Acknowledgements

Thanks to Jordi Llinares and the orphan team at EMA for the work and the slides

Thanks to Prof Kerstin Westermark, Chair of the EMA Committee for Orphan Medicinal Products

# What is the EMA?

An Agency of the European Union responsible for the scientific evaluation of **medicines** for human and animal use in the European Union (European Network):

- **Orphan Designation** for medicines for rare diseases*
- Scientific Advice*
- Paediatric activities*
- Marketing Authorisations and variations
- Inspections
- Innovation, methodology and statistics*
- Pharmacovigilance
- Article 58 with WHO
- SME office*


London, Canary Wharf
EMA
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# Outline

Overview orphan designation

Procedure and criteria

- Definition of a medical entity
- Significant benefit
- Outcomes
- Other activities
- Transparency

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# Why an orphan regulation?

Rare diseases → developing and marketing cost would not be recovered by the expected sales

Pharmaceutical industry does not develop medicines for rare diseases under normal market conditions

Persons suffering from rare conditions deserve treatment and same quality of medicines as other patients

# Objectives of the European Regulation

- Provide incentives that stimulate research and development (push)
- Modify market conditions (pull)

- Set up a system of recognition of orphan medicines entitled to incentives
- Since 2000

# Legal references 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

Implementing **Commission Regulation** (EC) No 847/2000 of 27 April 2000

Supplemented by:

Commission communication July 2003 (2003/C 178/02)

Commission communication on Art 8(1) and (3) (C(2008) 4077)

# Main characteristics of orphan designation

For medicinal products for human use

Procedure free of charge, at EMA only:

- Can be requested at any stage of development

Sponsor can be either company or individual:

- Established in the European Union or EEA/EFTA (Ice, Liech, Nor)

Scientific opinion given by Orphan Committee (COMP)

European Commission makes Decision, which gives access to incentives

# Incentives (1)

## Fee reduction / exemptions

- Extended incentives for Small and Medium Sized Enterprises!

➔ free protocol assistance

➔ free marketing authorisation application

➔ free post authorisation application and annual fee during first year from authorisation

Protocol Assistance

# Incentives (2)

10-year **market exclusivity** (+ 2 for paediatric development)

- Protection against similar products
  - Same molecular structure
  - Same mechanism of action
  - Same granted indication
- 3 derogations (allowing access to market when similar)
  1. Sponsor's consent
  2. Lack of supply
  3. Clinical superiority

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# Designation criteria

**RARITY (prevalence) or RETURN ON INVESTMENT**

Medical condition affecting no more than 5 in 10,000 persons in the European Union (around 250,000 patients affected)

or

Without incentives it is unlikely that the marketing of the product would generate sufficient return to justify the necessary investment

**AND SERIOUSNESS**

Life –threatening or chronically debilitating

**AND NO SATISFACTORY METHODS AUTHORISED**

If satisfactory method exists, the sponsor should establish that the product will be of **SIGNIFICANT BENEFIT**

# Committee for Orphan Medicines (COMP)

1 Representative per Member State (27)

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

and 1 elected Chair (Prof. Kerstin Westermark)

As needed, experts and Observers

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# ‘Medical condition’ for Orphan designation

Defined in European Commission Guideline:

- Any deviation 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)

Examples:

*Duchenne Muscular Dystrophy*

*Gaucher disease*

*Mesothelioma*

# Additional considerations on 'condition'

- Distinct entity if justified by pathophysiology, histology, clinical presentation
- Development is plausible based on pathogenesis and pharmacodynamics

However:

- Different severities or stages of a common disease not acceptable:

  *Second-line treatment of …*

  *Patients refractory to …*

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# Significant benefit – EU specifics

"A clinically relevant advantage or a major contribution to patient care"

- Based on assumptions at the time of orphan designation
- Shown over authorised products (=satisfactory methods), but comparative data not always required
- Significant benefit (and other orphan criteria) to be confirmed (data) prior to marketing authorisation
- COMP has worked on a Recommendation for the data on Significant Benefit and medical plausibility

# ‘Assumption’ of Significant Benefit

- Medicine has a new mechanism of action leading to
  - Better effect and potential better/greater efficacy (still to be demonstrated)
  - Opens possibilities for drug combinations, and broadens therapeutic alternatives
- More convenient administration route (= major contribution to patient care)
  - When documented problems exist with existing route
- Complementary (better) safety profile
  - Weak justification of significant benefit (which data to support?)

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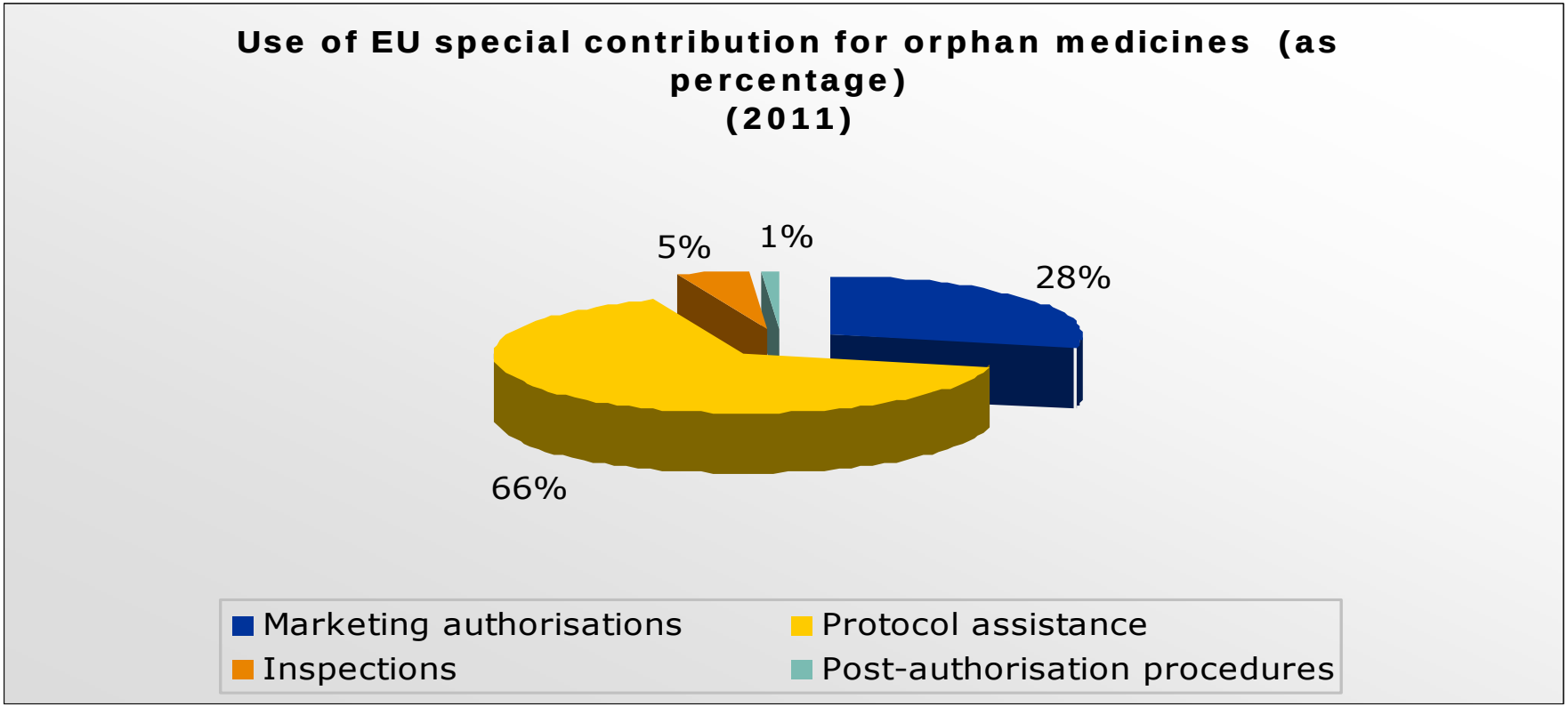
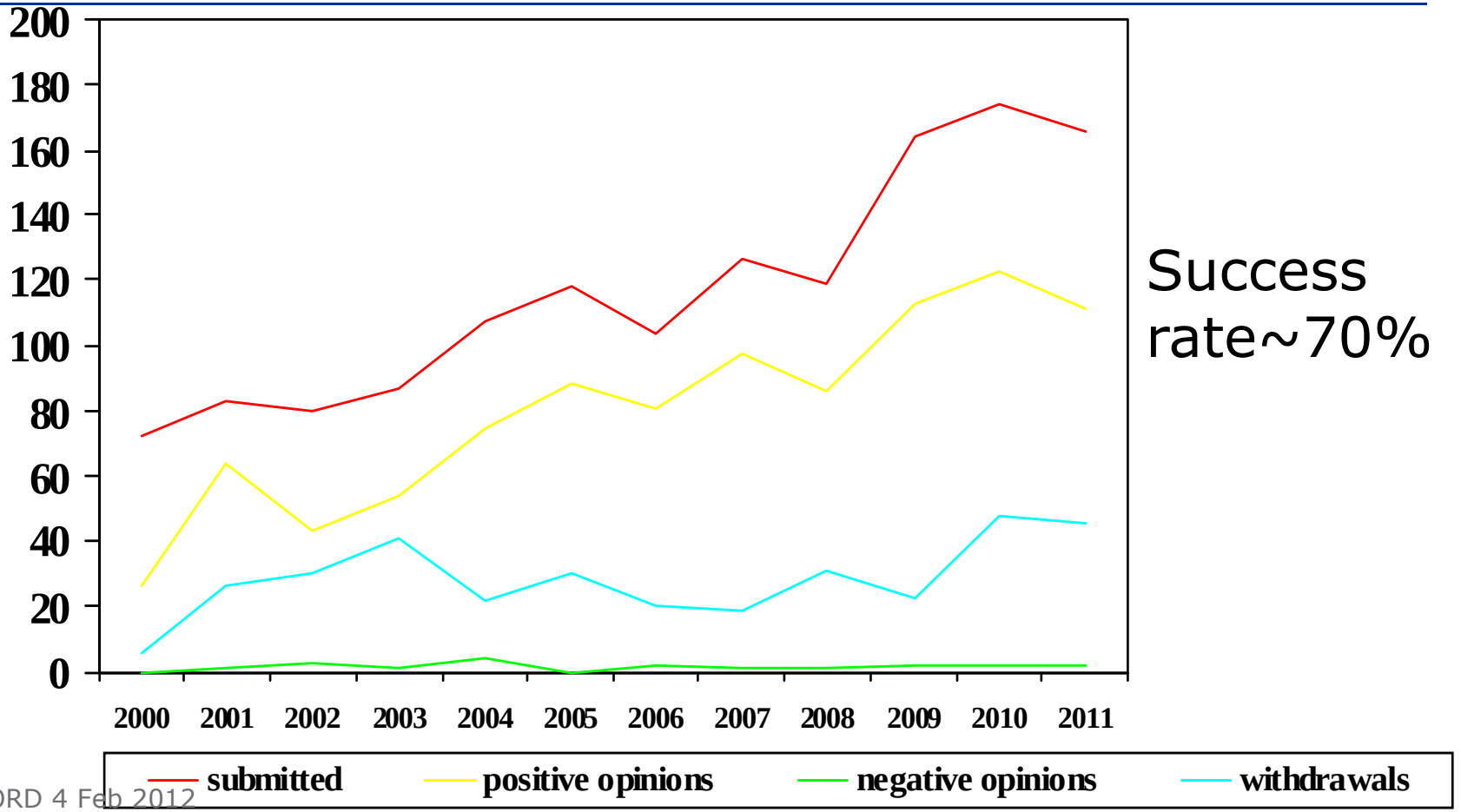
# Use of EU subsidy (not fees from industry)



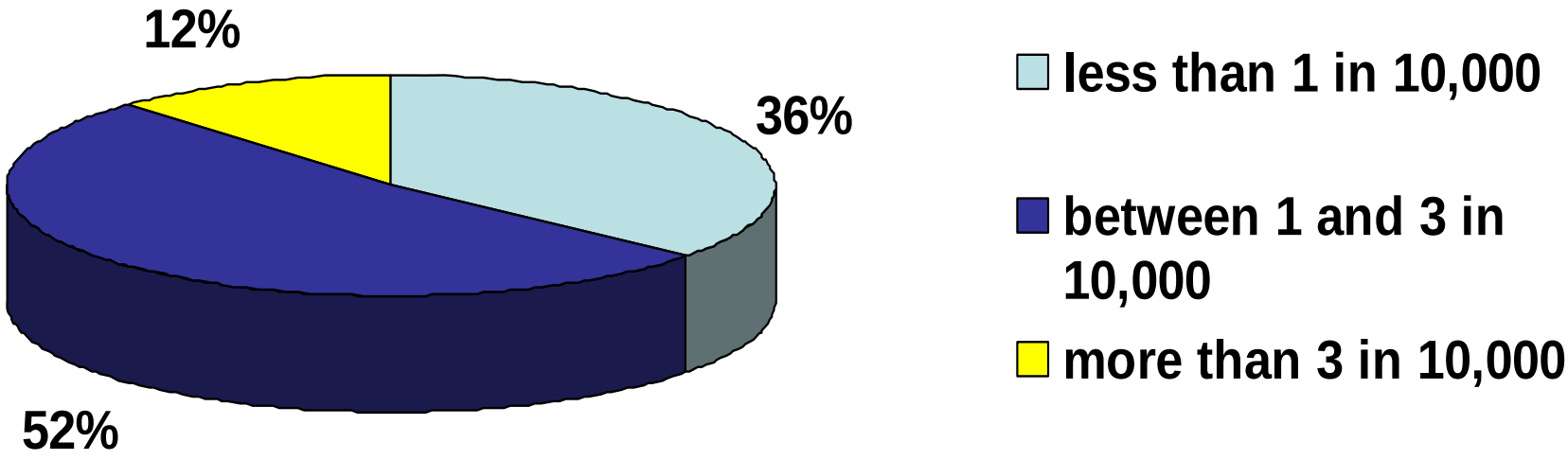

Use of ≈ 6 million Euro per year

# Outcome of orphan designation

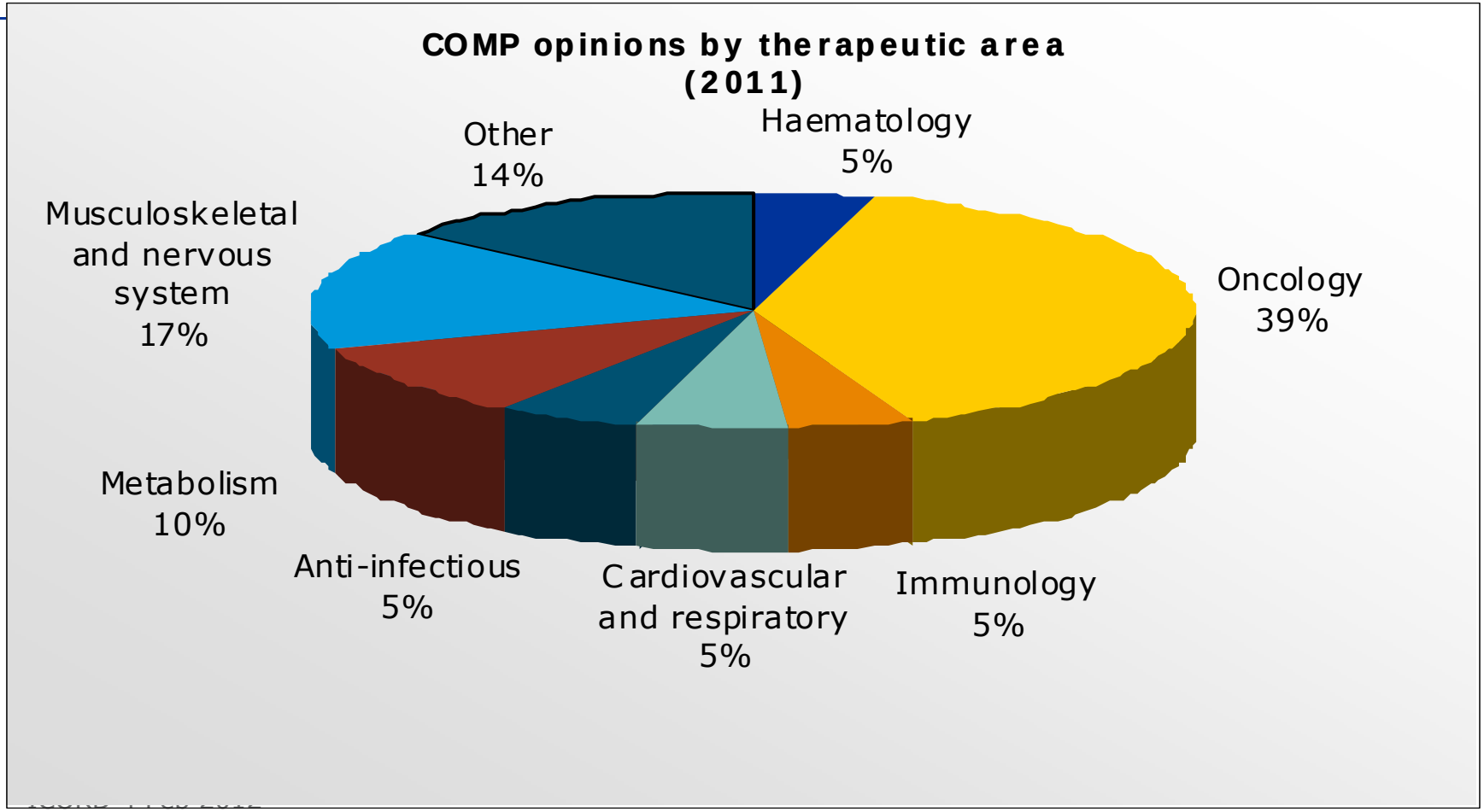



Success rate~70%

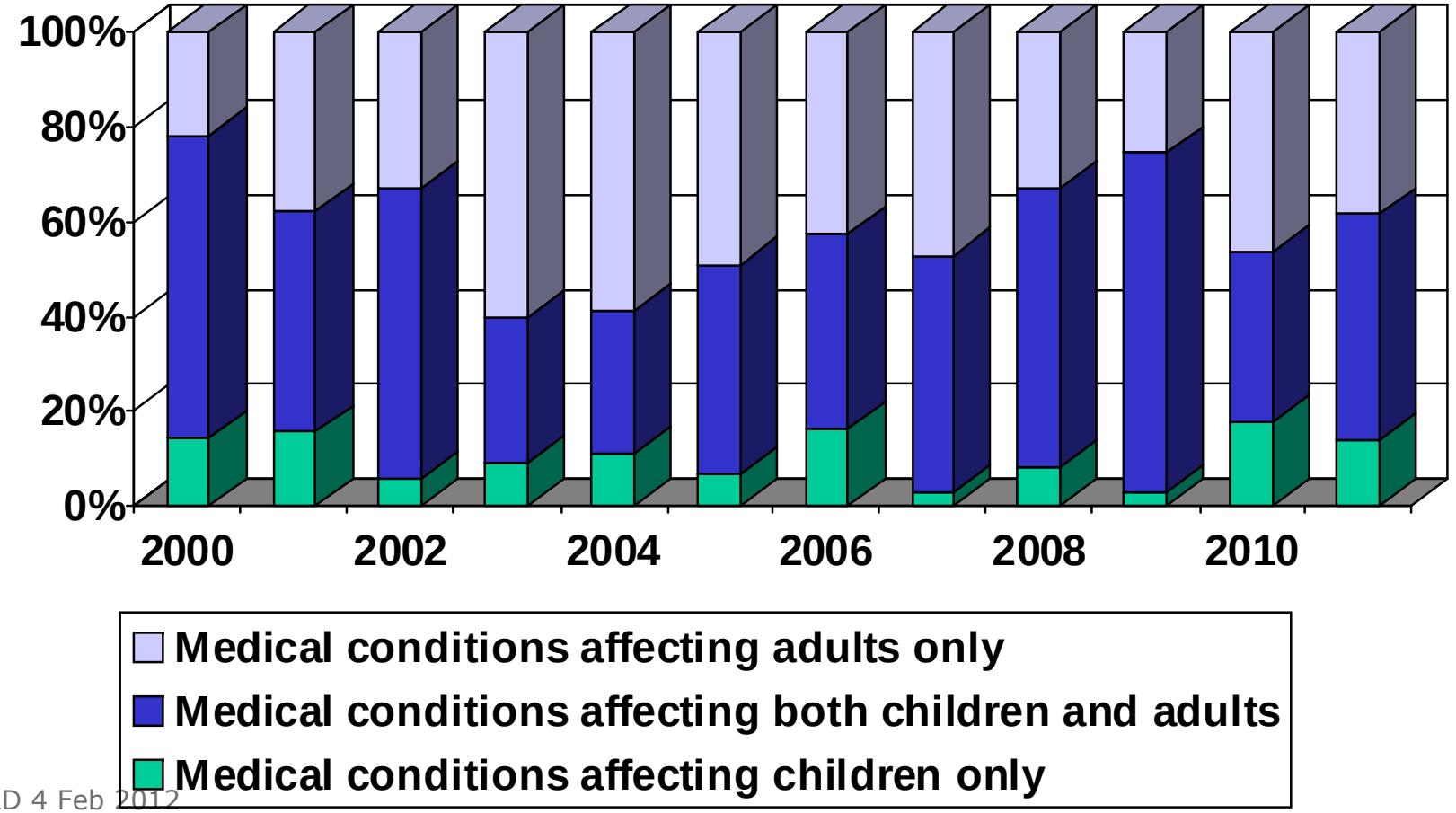
# Orphan Designations and Prevalence



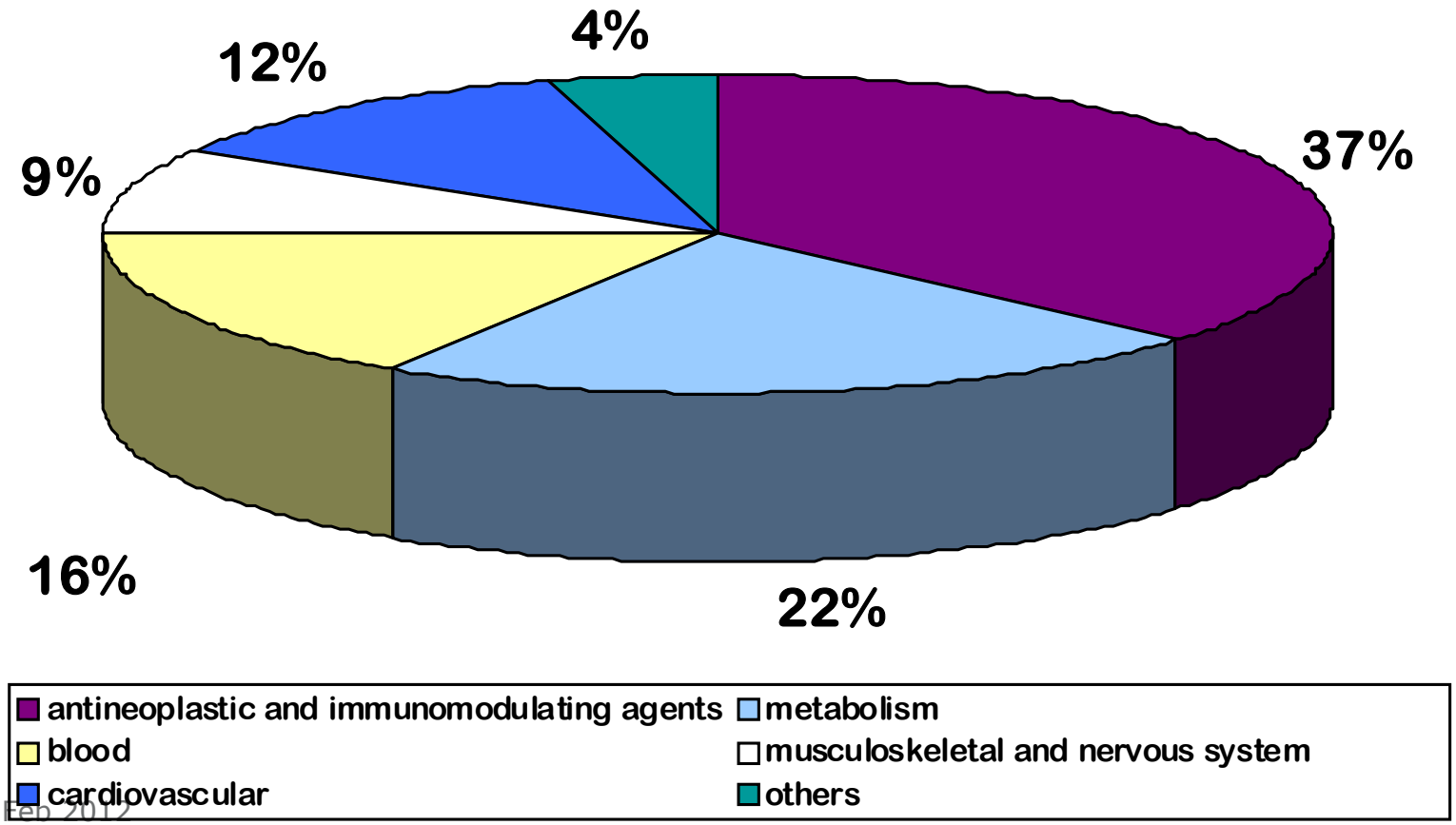
# Orphan Designation by therapeutic area



# Orphan Designation for paediatric conditions



# Orphan products **authorised** per therapeutic area (n=69)



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# Transparency of Orphan designations

- COMP monthly report (Opinions)
- EU Commission Register of orphan designated medicinal products (Decisions)
- Public summary of positive/negative opinion for orphan designation (at time of Decisions)
- Summary of review of orphan designation at time of Marketing Authorisation (since 2010) – Link with European Public Assessment Report

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# EU/3/10/752



Orphan designation | Key facts | Review of designation

On 6 June 2010, orphan designation (EU/3/10/752) was granted by the European Commission to Shire Pharmaceuticals Ireland Limited, Ireland, for velaglucerase alfa for the treatment of Gaucher disease.

Expand all items in this list

- What is Gaucher disease?
- What is the estimated number of patients affected by the condition?
- What treatments are available?
- How is this medicine expected to work?
- What is the stage of development of this medicine?
- Opinions on orphan medicinal product designations are based on the following three criteria:

| Name | Language | First published | Last updated |
|---|---|---|---|
| EU/3/10/752: Public summary of positive opinion for Velaglucerase alfa for the treatment of Gaucher disease | (English only) | 23/06/2010 | 18/10/2010 |

**Related information**

Vpriv: EPAR

**Sponsor's contact details:**

Shire Pharmaceuticals Ireland Limited
5 Riverside Walk
Citywest Business Campus
Dublin 24
Ireland
Telephone: +353 1 4297700
Telefax: +353 1 4297701

# International collaboration on rare diseases

Rare diseases share common needs / challenges (rationale for international approach)

Orphan medicines are developed at a global level

- Expertise is scarce and scattered
- Efficient use of resources
  - Low number of patients and geographically dispersed
  - Multi-centre/national trials (centres of reference)

Designation done in parallel or close in time

- Global market
- Pooling incentives

# Collaboration in orphan designation

## Administrative simplification

- Relatively simple and cost efficient
- Facts (US-EU):
  - common application form and common application format
  - Single submission of annual reports

## Communication-collaboration during assessment

- Analysis of reasons for divergent opinions
- Sharing of information in real time: monthly teleconferences (regulatory experience)
- Sharing experts

# Collaboration during medicine development

## Scientific advice

- Parallel advice EU-US established
- Global development requires consistent/compatible advice (at least not contradictory!)
- Issues of trials and endpoints

## Safety information exchange

# Collaboration post authorisation

## Safety issues / pharmacovigilance

- Sharing information on signals and alerts
- Adoption of similar measures (in the FUTURE?)

## Establishment of common registers (in the FUTURE?)

- Coordination to avoid duplication / waste of resources
- Register structure should allow combination of data

# The first steps already in place

Confidentiality arrangements

- EU-FDA
- EU-Japan
- EU-Canada
- EU- Australia

International liaison officers posted

Exchange of staff

Clusters for therapeutic areas, for orphan medicines, paediatrics, pharmacovigilance, etc.

- Monthly teleconferences
- Common projects

# Establishment of a network of regulators for Orphan medicines

PROPOSAL:

Discussion and exchange forum

Stimulation of orphan policies in other countries

Need to agree on practical and realistic deliverables

Network that takes advantage of modern communication tools

Chair → Rota every 2 years?

# Proposals for the network (1)

Promotion of orphan designation by

- Increasing awareness about designation procedures and incentives
- Increasing dialogue and understanding about designation criteria
- Administrative simplification within and between regulatory authorities
- Promoting existing incentives for orphan medicines
- Finding an advocate for medicine development for rare diseases in each regulatory authority

# Proposals for the network (2)

Promotion of development of medicinal products for rare diseases

- Monitoring of current development of medicinal products for rare diseases
- Identification of unmet development needs
- Joint recommendations on the development of concrete measures to support – incentivise drug development

# The Pediatric medicines Regulatory Network (PmRN) of WHO

Following ICDRA in 2008,

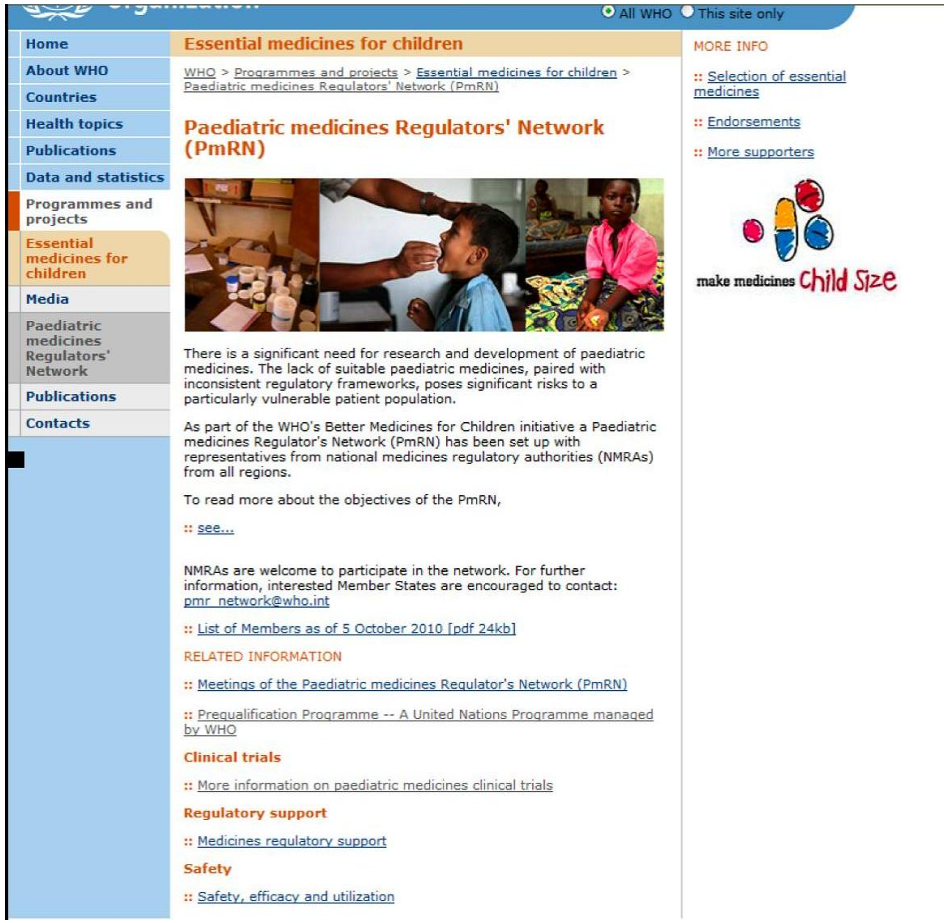
a network was created:

26 NRAs are participating.

Monthly teleconferences

Exchange of information

Identify gaps and contribute to capacity building



# Conclusions

ICORD is perfect opportunity to create a network of regulators

Raising awareness of orphan incentives across the world

Collaboration on difficult medicines development

Questions on Orphan Medicines and Designation to:

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