# The role of EMEA in Orphan Drug Development

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# The European Medicines Agency

- EMEA is the European Union body responsible for the evaluation and supervision of medicines in Europe.
- Its main responsibility is the protection and promotion of public and animal health.
- The EMEA works as a network, bringing together the scientific resources of the Member States.
- The Agency cooperates closely with international partners on a wide range of regulatory issues (e.g. ICH, WHO, FDA, etc)
- The Agency was created in 1995 and is headquartered in London.

# Drug Therapy in Rare Diseases

Persons suffering from rare diseases have the same rights as their fellow citizens to safe and effective therapies

# Orphan Regulations

- Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products of 16 December 1999

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

# What is an Orphan Medicinal Product

Orphan Medicinal Products

- for rare diseases (affecting less than 5 in 10,000 persons)
- development costs > expected return on investment
- life-threatening or very serious

Lack of sponsors developing orphan medicinal products

# What are the EU incentives ?

## Protocol Assistance
free scientific advice
to optimise development

## Market Exclusivity
for 10 years after grant of
EU marketing authorisation

## Centralised Procedure
direct access to EMEA
centralised procedure for
marketing authorisation

## EU-Funded Research
grants from Community
& Member State programmes

## Fee Reductions
reduction of centralised
regulatory fees via a special fund
from EU budgetary authority

# Application for Orphan Designation

Application should demonstrate orphan criteria have been met:

- life-threatening or debilitating nature of condition
- medical plausibility
- prevalence < 5 in 10,000 or unlikely to generate sufficient return on investment
- no satisfactory methods exist or medicinal product will be of significant benefit

All claims should be substantiated by references

# Committee for Orphan Medicinal Products (COMP)

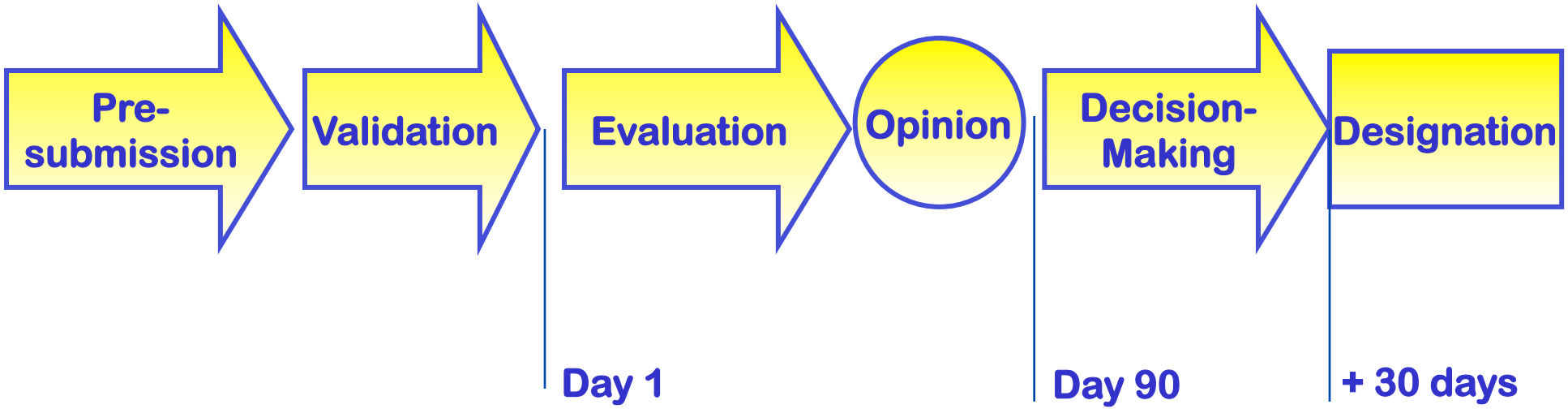
**EMEA Committee: 31 members + Chairman**

- 1 Member per Member State
- 3 representatives from patients groups
- 3 members proposed by the EMEA

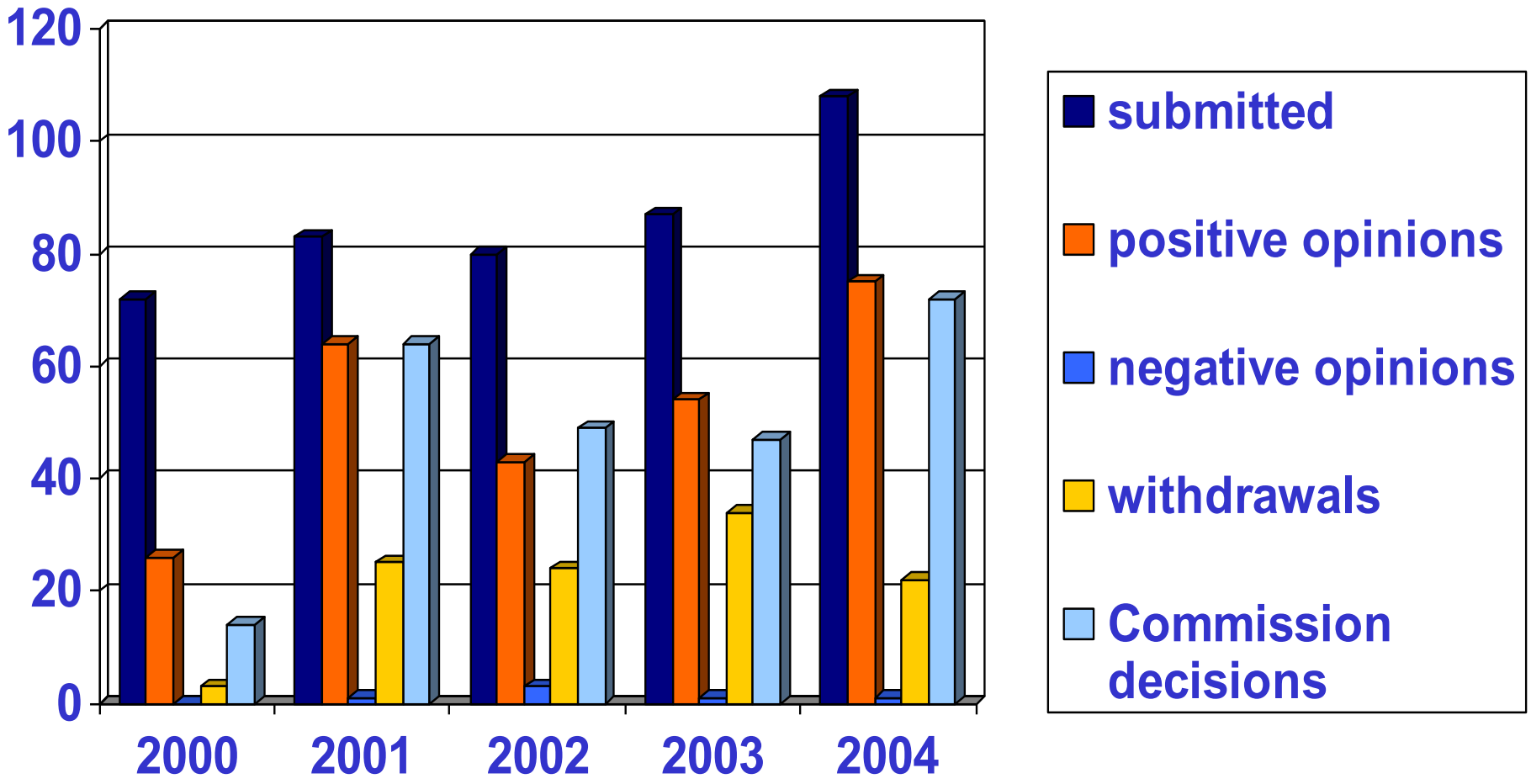
**COMP responsible for:**

- opinions on designation
- advising on general EU policies
- international co-operation

# Procedure for Orphan Designation

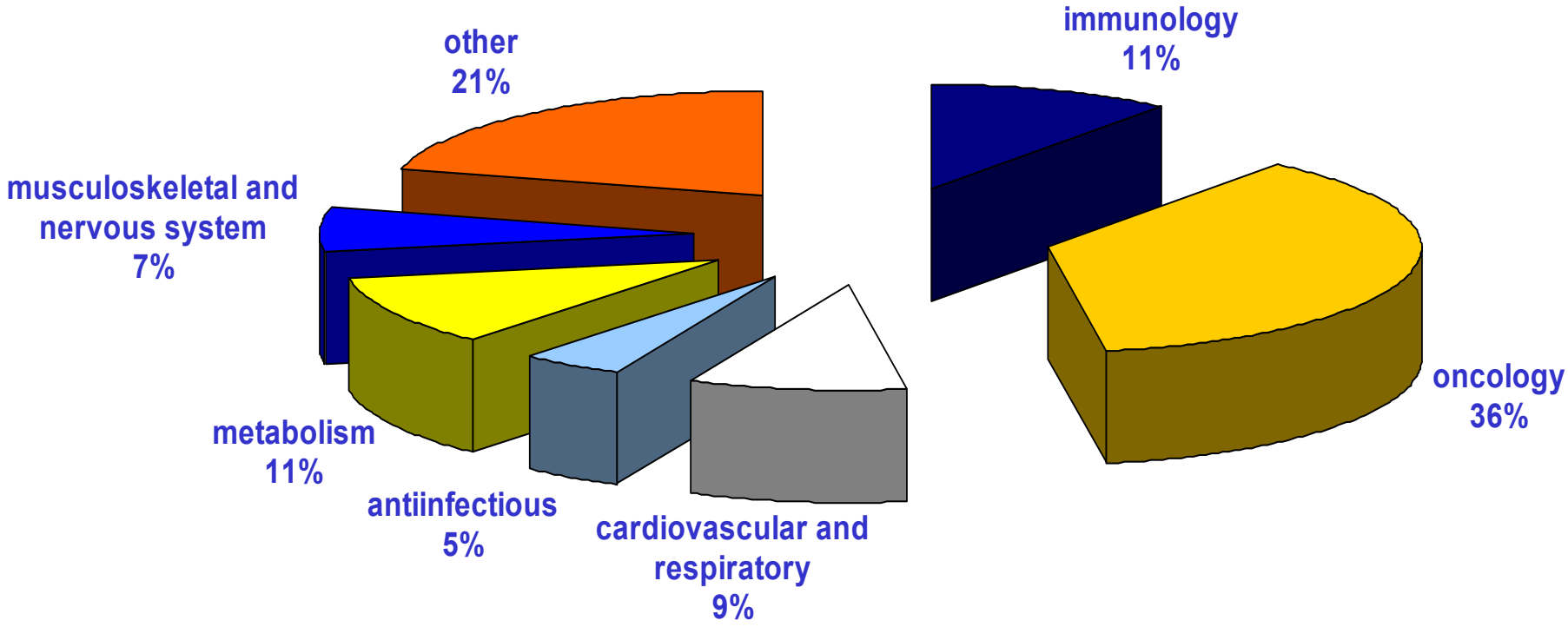


# Status of Orphan Applications




Up to January 2005

# Distribution of opinions




## Up to December 2004

# Opinions designated based on significant benefit

- Up to January 2005: 182 out of 262 opinions (69%) based on assumption of significant benefit over authorised treatments in the orphan condition
- Significant benefit to be reviewed at the time of Marketing Authorisation to maintain orphan status

# Protocol Assistance

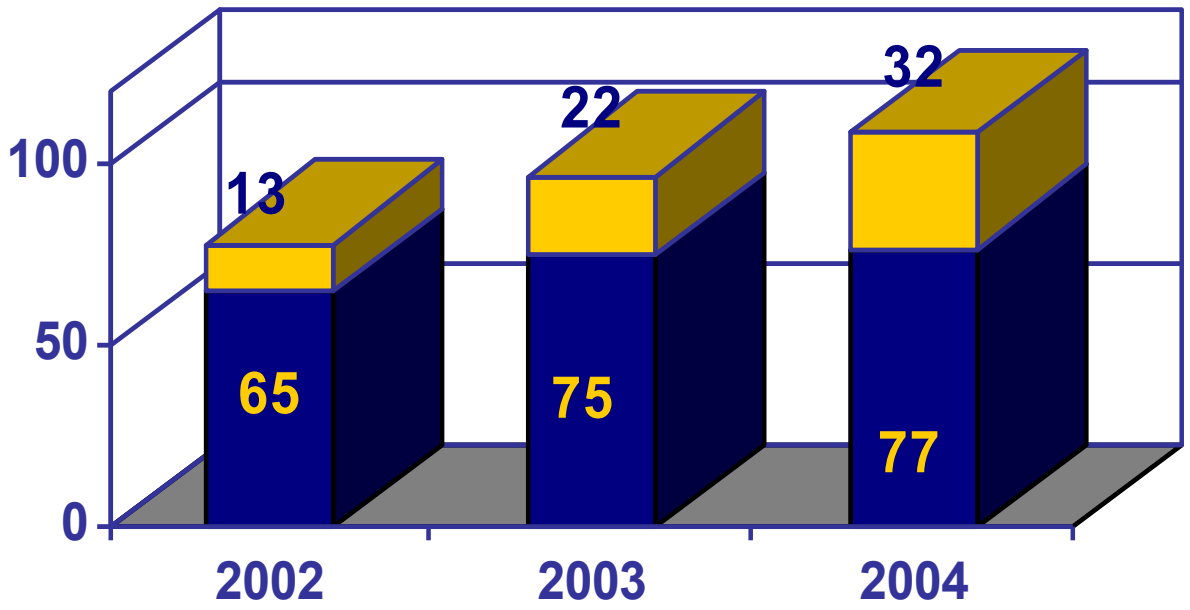
Article 6 of Regulation (EC) No 141/2000

- Protocol Assistance = Scientific Advice for companies developing Orphan Medicinal Products
- Revised procedure adopted by the CHMP 2003
- Implementation of changes from new Pharmaceutical Regulation by end 2005

# Protocol Assistance – Key Features

- Systematic pre-submission meeting with the EMEA
- Oral explanations in the majority of cases
- Additional and specific expertise to participate in SAWP
- Involvement of 2 representatives of the Committee for Orphan Medicinal Products in SAWP (Significant Benefit issues)
- Fee reduction (currently 100% = free)

# Scientific Advice / Protocol Assistance
## *Procedures*



# Orphan Medicinal Products
# Application for Marketing Authorisation (MAA)

## At the stage of MAA:

- Filing can currently be through Mutual Recognition Procedure or Centralised Procedure
- To obtain Market Exclusivity MA must be granted by all Member States in Mutual Recognition
- In November 2005, Centralised filing obligatory
- Fee reductions are granted by some MS's and by EMEA for centralised applications

# Status of Orphan Marketing Authorisation Applications

18 authorisations granted to date

- Fabrazyme for Fabry disease
- Replagal for Fabry disease
- Glivec for chronic myeloid leukaemia
- Tracleer for pulmonary arterial hypertension
- Trisenox for acute promyelocytic leukaemia
- Somavert for acromegaly
- Zavesca for Gaucher disease
- Carbaglu for hyperammonaemia

# Status of Orphan Marketing Authorisation Applications cont'd

- Aldurazyme for Mucopolysaccharidosis
- Busilvex for haematopoietic progenitor cell transplantation
- Ventavis for pulmonary arterial hypertension
- Onsenal for Familial Adenomatous Polyposis
- Litak for Hairy cell leukaemia
- Lysodren for adrenal cortical carcinoma
- Pedea for Patent Ductus Arteriosus
- Photobarr for Barret's oesophagus
- Wilzin for Wilson's disease
- Xagrid for Thrombocythaemia

# Status of Orphan Marketing Authorisation Applications cont'd

**Two CHMP Opinions in decision-making**

- Orfadin for Hereditary tyrosinemia type 1
- Prialt for chronic pain

**Three extensions of indication**

- Glivec for Gastrointestinal Stromal Tumours
- Glivec for first line use in Chronic Myeloid Leukaemia
- Glivec for paediatric use in Chronic Myeloid Leukaemia

**Nine centralised applications in review process**

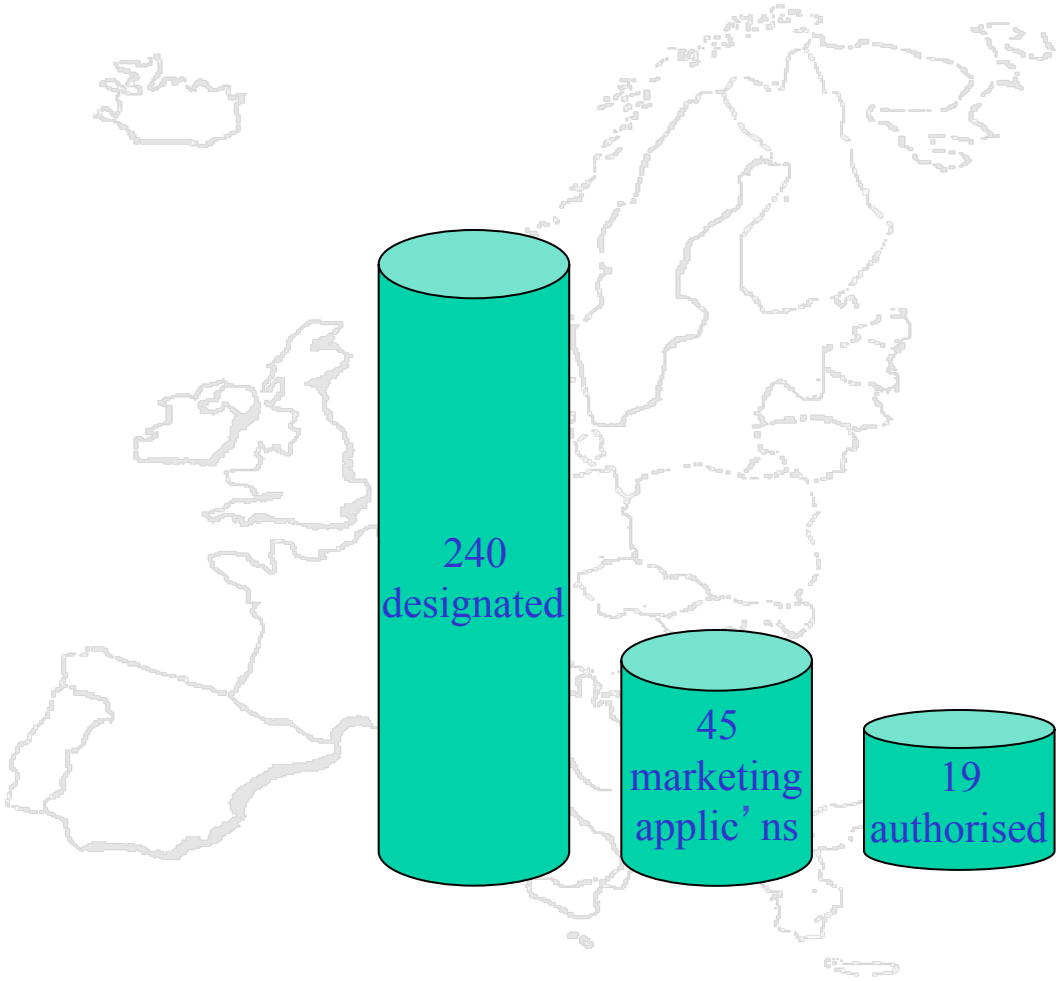
**Four applications filed through Mutual Recognition**

# Overview of “evidence” in authorised products

- Data provided
  - in 28% of products phase III studies (double blind, randomised, placebo controlled)
  - in 44% of products phase II studies

- 61% of Marketing Authorisations granted under “exceptional circumstances”

# Orphan Marketing Authorisations




830,000 patients