Allgemeine Rahmenbedingungen für die Entwicklung und Zulassung von Orphan Medicinal Products

PMS-Workshop
Arzneimitteltherapie seltener Krankheiten – Herausforderungen und Chancen

Berlin-Brandenburgische Akademie der Wissenschaften
Berlin, 25. Januar 2007

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Drug Therapy in Rare Diseases

Persons suffering from rare diseases have the same rights as their fellow citizens for treatment options with safe and effective therapies

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Drug Therapy in Rare Diseases – Consequences

Pharmaceutical companies are unwilling to develop such medicinal products under normal market conditions, as the cost of bringing them to the market would not be recovered by the expected sales of the medicinal products without incentives.

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What is an Orphan Medicinal Product?

Orphan Medicinal Products

- for rare diseases
- life-threatening or very serious
- development costs exceeding expected return on investment

Lack of sponsors developing orphan medicinal products

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Orphan International Overview

- United States 'Orphan Drug Act' 1983
  - 1200 designations
  - 220 marketing authorisations
- Japan 'Orphan Drug Legislation' 1993
- Singapore 'Orphan Legislation' 1997
- Australia 'Orphan Legislation' 1998
- Europe 2000
  - 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

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Medicinal and Orphan Products Legal Basis

Legal Basis Medicinal Products

- Council Directive 2001/83/EC amended by 2002/98/EC, 2003/24/EC and 2003/27/EC
  - Annex 1 (2003/63/EC)
- Commission Regulation (EC) 1084/2003 & 1085/2003
- Regulation (EC) 726/2004
  - Annex (to enter into force 20.11.2005 and 20.05.2008)

2003/94/EC (GMP), 87/18/EEC & 88/320/EEC (GLP)
86/609/EEC (animals), 2001/20/EC (GCP)

- European Pharmacopoeia

Legal Basis Orphan Products (in addition to the above)

- EUROPEAN PARLIAMENT and COUNCIL REGULATION (EC) No 141/2000
  - Commission Communication on orphan medicinal products 01/08/2003
- COMMISSION REGULATION (EC) No 847/2000

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Orphan Products - Scope of EU Regulations

- For medicinal products for human use only
  - Not for medical devices
  - Not for food or food supplements
  - Not for medicinal products for veterinary use

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Criteria for Orphan Designation

- medically plausible condition
- life-threatening or debilitating nature of condition
- 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

International Comparison – Difference Europe and USA

- **Europe:** „Significant Benefit“ requirement
- **USA:** No such requirement

Orphan Medicinal Products Designation vs. Authorization (1)

Designation - providing incentives for the development of medicinal products for the benefit of patients suffering from rare conditions

Authorization - ensuring that only medicinal products that are effective, safe and of good quality are marketed

(in general, Orphan Medicinal Products require the same level of evidence with regard to the risk / benefit for marketing authorization as non-orphan products. However, there are some special considerations possible like e.g. authorization under exceptional circumstances)

Orphan Medicinal Products
Designation vs. Authorization (2)

Level of Evidence:

Designation	**- reasonable scientific assumptions**
Authorization	**- scientifically proven facts**

COMP Composition

The Regulation establishes the Committee for Orphan Medicinal Products (COMP), within the EMEA, which is responsible for examining all applications for orphan medicinal product designation submitted to it in accordance with the Regulation (Reg. No 141/2000).

33 voting, 2 non-voting Members:

- one member nominated by each the Member State (27)
- three members nominated by the Commission to represent patient's organisations (3)
- three members nominated by the Commission on the basis of a recommendation from the Agency (3)
- two non-voting members (IS, NO) (& further observers)

Orphan Medicinal Products in the EU

The Incentives (non exhaustive)

- Market exclusivity
- Protocol assistance during the development, with involvement of the CHMP
- Fee reduction for centralised applications (and marketing authorisation maintenance activities)
- Priority access to EU research programs
- National incentives (grants, tax reductions)
- (Shorter time to market)
- (To attract venture capital)

Orphan Medicinal Products in the EU

Market Exclusivity

- Period of ten years exclusivity from the date of marketing authorisation
- Conditions:
  orphan designation
  AND marketing authorisation throughout EU
- Scope of exclusivity:
  no market authorisation for
  similar medicinal products
  in the same indication(s)

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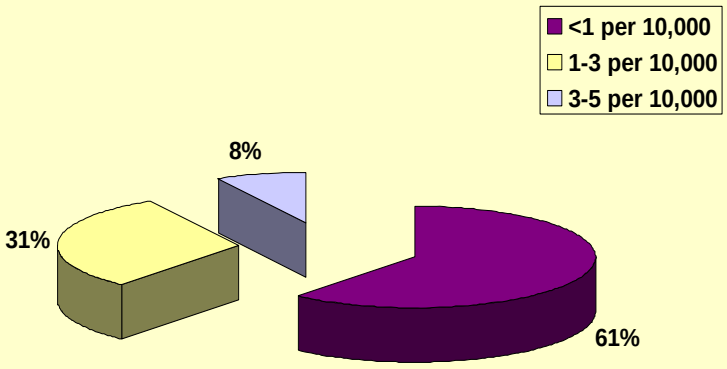
Prevalence



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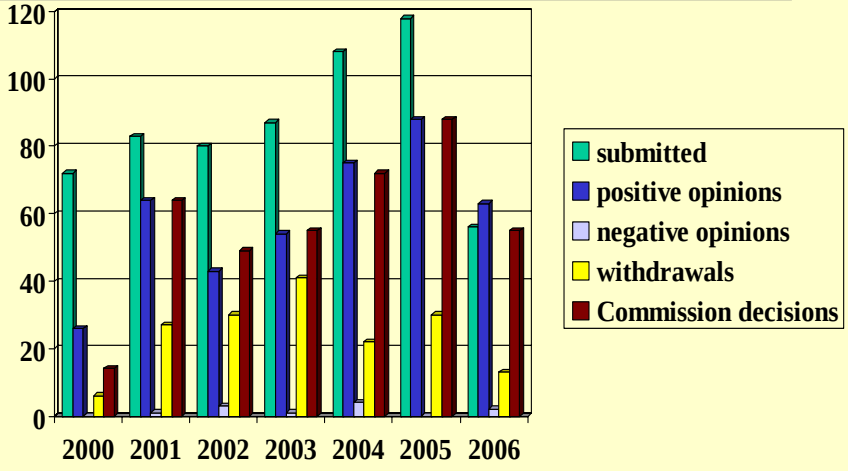
Status of Orphan Applications



Up to 7 September 2006

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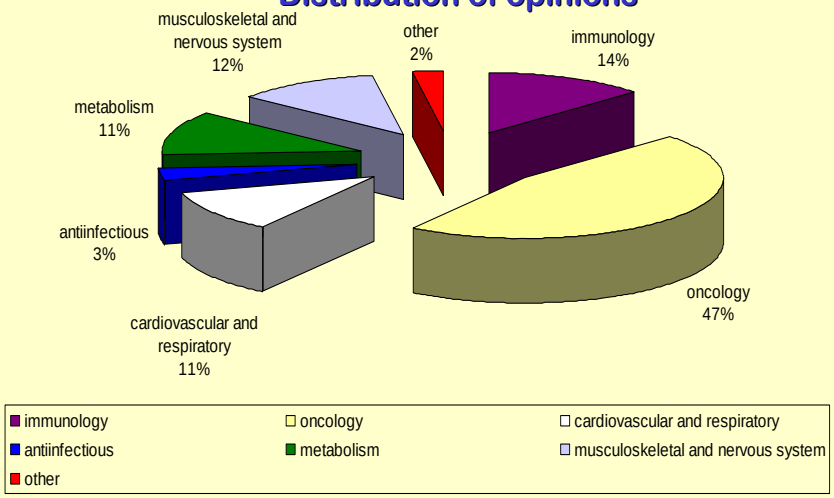
Distribution of opinions



Up to 7 September 2006

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Reservefolien

Status of Orphan Applications

	2000	2001	2002	2003	2004	2005	2006	Total
No. of applications submitted	72	83	80	87	108	118	75	623
Positive COMP Opinions	26	64	43	54	75	88	63	413
Commission Decisions	14	64	49	55	72	88	55	397
Final Negative COMP Opinions	0	1	3	1	4	0	2	11
Withdrawals	6	27	30	41	22	30	13	169

Up to 7 September 2006

Orphan Medicinal Products in the EU

The Procedure

A sponsor submits the application to the EMEA *

↓

the EMEA validates the application (day 1)

↓

the COMP / EMEA prepares a summary report

↓

the COMP adopts an Opinion (max. by day 90)

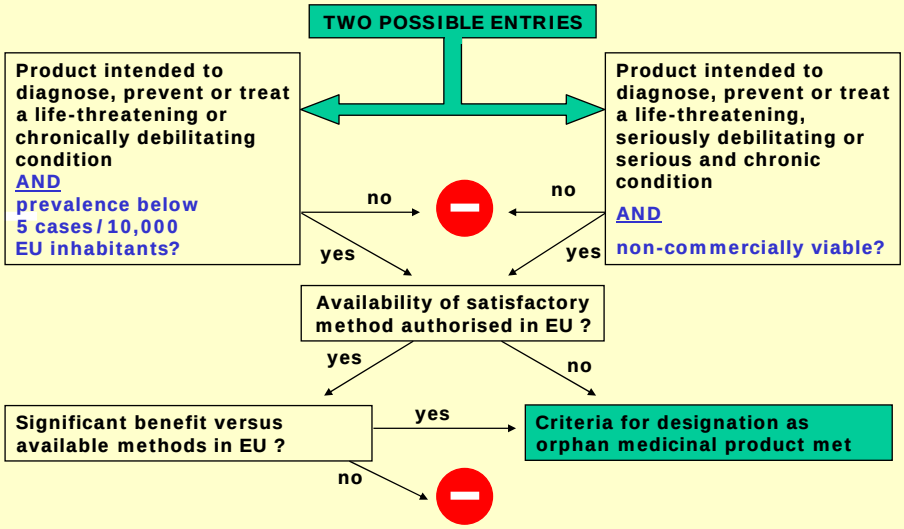
↓

the EU Commission adopts a Decision (30 days)

* Pre-submission meetings with EMEA highly encouraged

Orphan Medicinal Products in the EU

Application:



Orphan Medicinal Products Apply When? (1)

A sponsor applying for designation of a medicinal product as an orphan medicinal product shall apply for designation at any stage of the development of the medicinal product **before** the application for marketing authorisation is made.

This means that if a marketing authorisation for the same medicinal product (in respect of the same therapeutic indication and submitted by the same sponsor) has already been submitted in any Member State within the Community, whether or not the marketing authorisation has been granted, that this medicinal product is no longer eligible for designation.

Orphan Medicinal Products
Apply When? (2)

A sponsor may apply for designation of a medicinal product as an orphan medicinal product for **an already approved medicinal** product provided the orphan designation concerns an unapproved therapeutic indication.

In this case, the marketing authorisation holder shall apply for a separate marketing authorisation which will cover only the orphan indication at the time of application for a marketing authorisation.

From: REGULATION (EC) No 141/2000
Article 8, Market exclusivity

Where a marketing authorisation in respect of an orphan medicinal product is granted pursuant to Regulation (EEC) No 230993 ..<cut>..the Community and the Member States shall not, for a period of 10 years, **accept another application** for a marketing authorisation, or **grant a marketing authorisation** or accept an application to **extend an existing marketing authorisation**, for the same therapeutic indication, in respect of a similar medicinal product.

Orphan Medicinal Products in the EU

The Role of the EMEA

- Validation and assessment of requests for designation
- Protocol assistance: regulatory and scientific
- Administrative & technical secretariat of COMP
- Publication of public summary of opinion
- EU Register on Orphan Drugs
- Fee reductions

COMP - CHMP Interaction

Applicant

EMEA

COMP | **CHMP**

Assessments
Follow up

Interaction with
Interested Parties

EMEA Experts

Experts for rare diseases

Scientific Advice

Review of Application

Opinion
Designation

EU Commission

Opinion
Marketing Auth.