

Seven Years of Orphan Drug Policy:

What's next?

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Why an EU Regulation on Orphan Drugs?

Extracts from EU Regulation 141/2000 on Orphan Medicinal Products:

“Patients suffering from rare conditions should be entitled to the same quality of treatment as other patients”

But...

“the pharmaceutical industry would be unwilling to develop the medicinal product under normal market conditions”

As...

“some conditions occur so infrequently that the cost of developing and bringing to the market a medicinal product (...) would not be recovered by the expected sales”

Criteria for Orphan Designation

- **SERIOUS CONDITIONS**
- **RARE** < 5/10.000 individuals in the EU
or
- **LACK OF RETURN ON INVESTMENT**
- **NO SATISFACTORY TREATMENT**
or
- **"SIGNIFICANT BENEFIT"**

Which incentives in EU for Orphan Drugs?

- **Market Exclusivity**
 - 10 years for all orphan medicines (from marketing authorisation)
 - *+ 2 years if paediatric studies performed*
- **Fee Reductions** for product development
 - Application for Orphan Designation: free
 - *Protocol assistance and follow up: free*
 - Application for Marketing Authorisation: reduced fees
 - *Extended incentives for SMEs in post authorisation*
- *EU Marketing Authorisation (unique centralised procedure)*
- **Priority** to EU Research - Framework programs
- **National incentives** (EC inventory)

COMP Tasks:

- Give opinions on orphan designation applications
- Advise the EU Commission on Orphan Drug Policy
- Assist the Commission in liaising internationally on orphan drugs and with patient groups
- Assist the Commission in drawing up guidelines

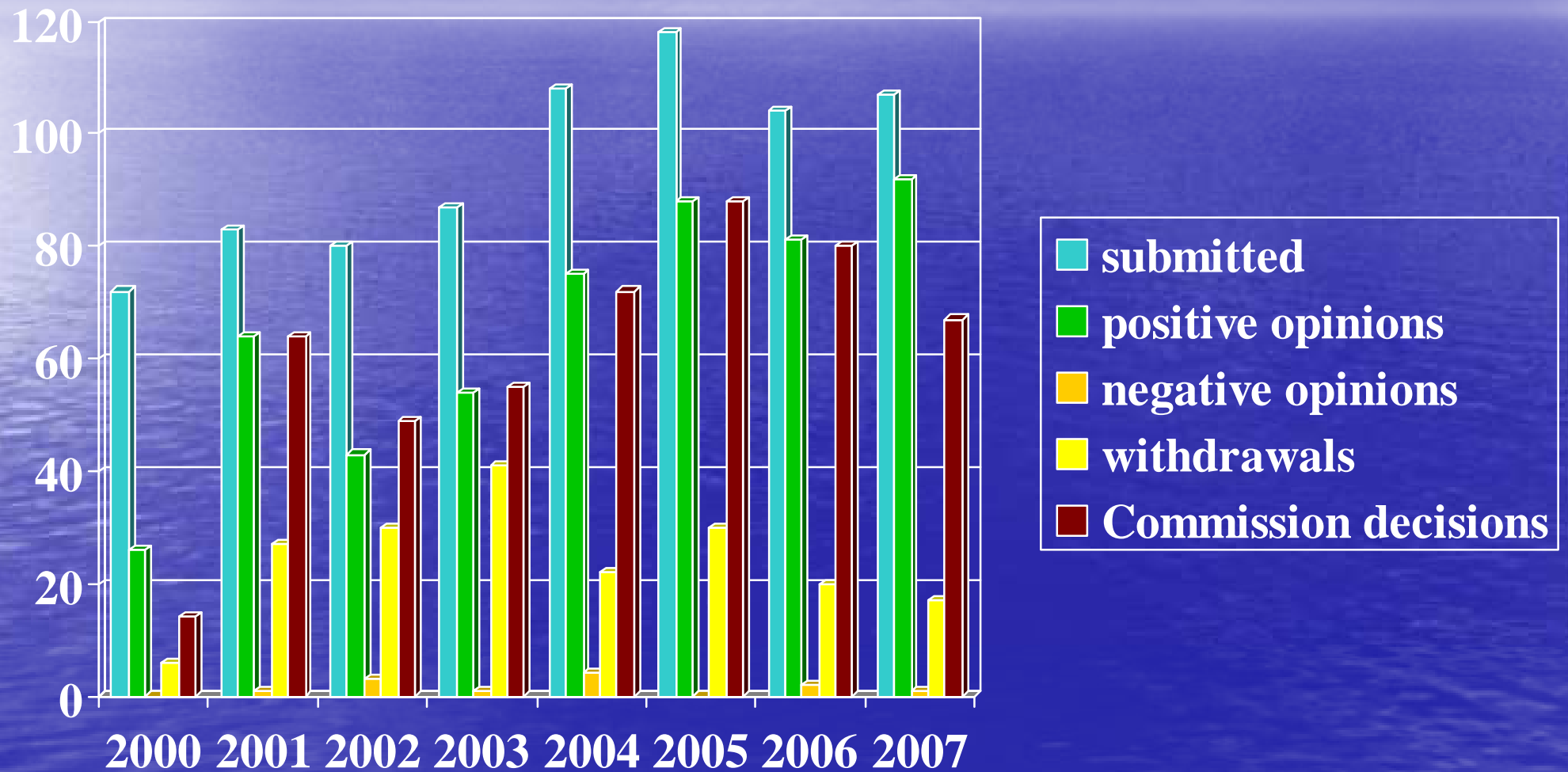
What was expected?

- c:a 15 orphan drug applications/year
- 4-5 one day COMP meetings/year

What was the result?

- c:a 100 applications/year
- 11 two day COMP meetings/year

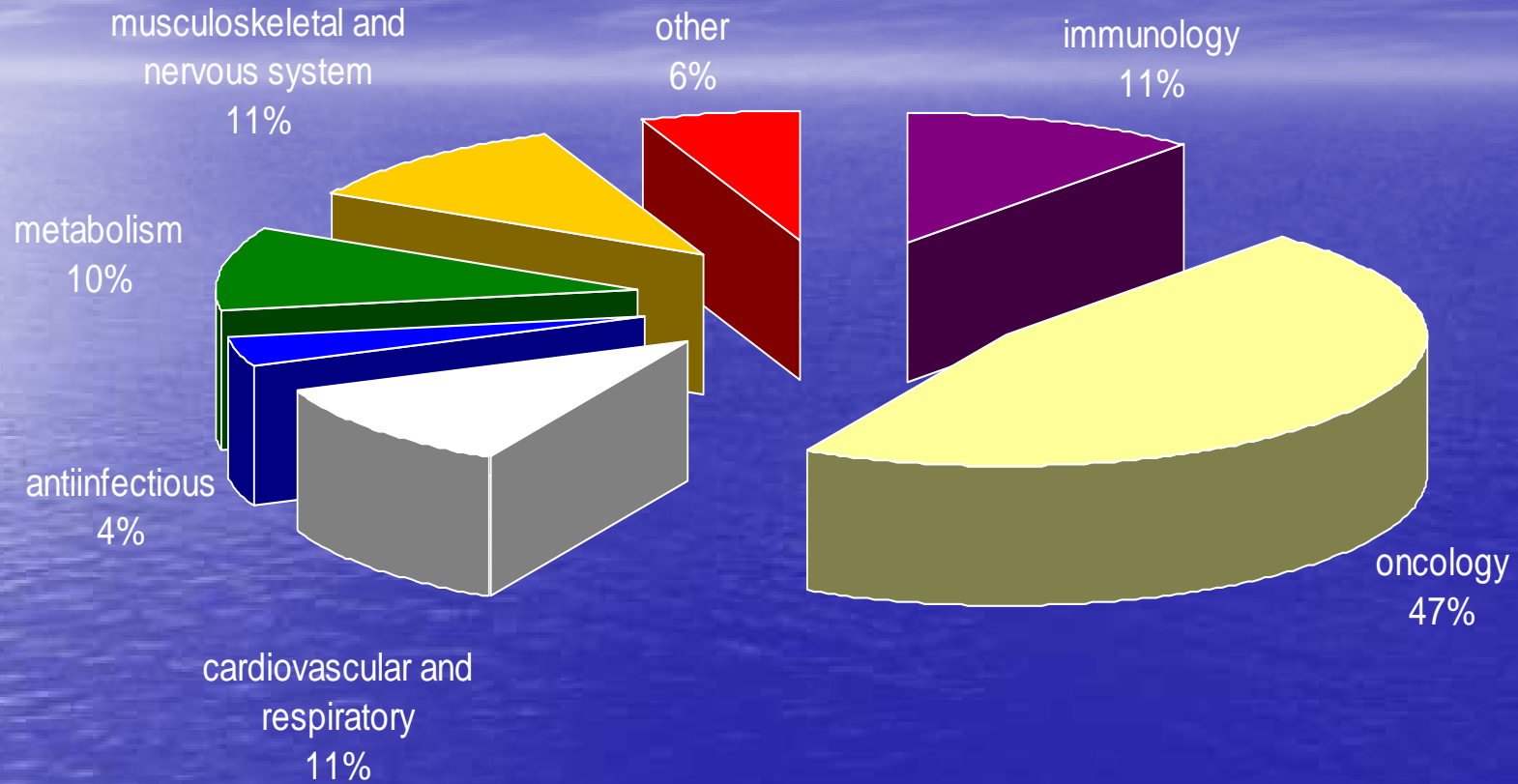
Status of Orphan Applications as of November 2007








Status of Orphan Applications as of November 2007

- 759 orphan drug applications submitted
- 523 positive opinions
- 193 applications withdrawn by sponsor
- 12 negative opinions/refusals

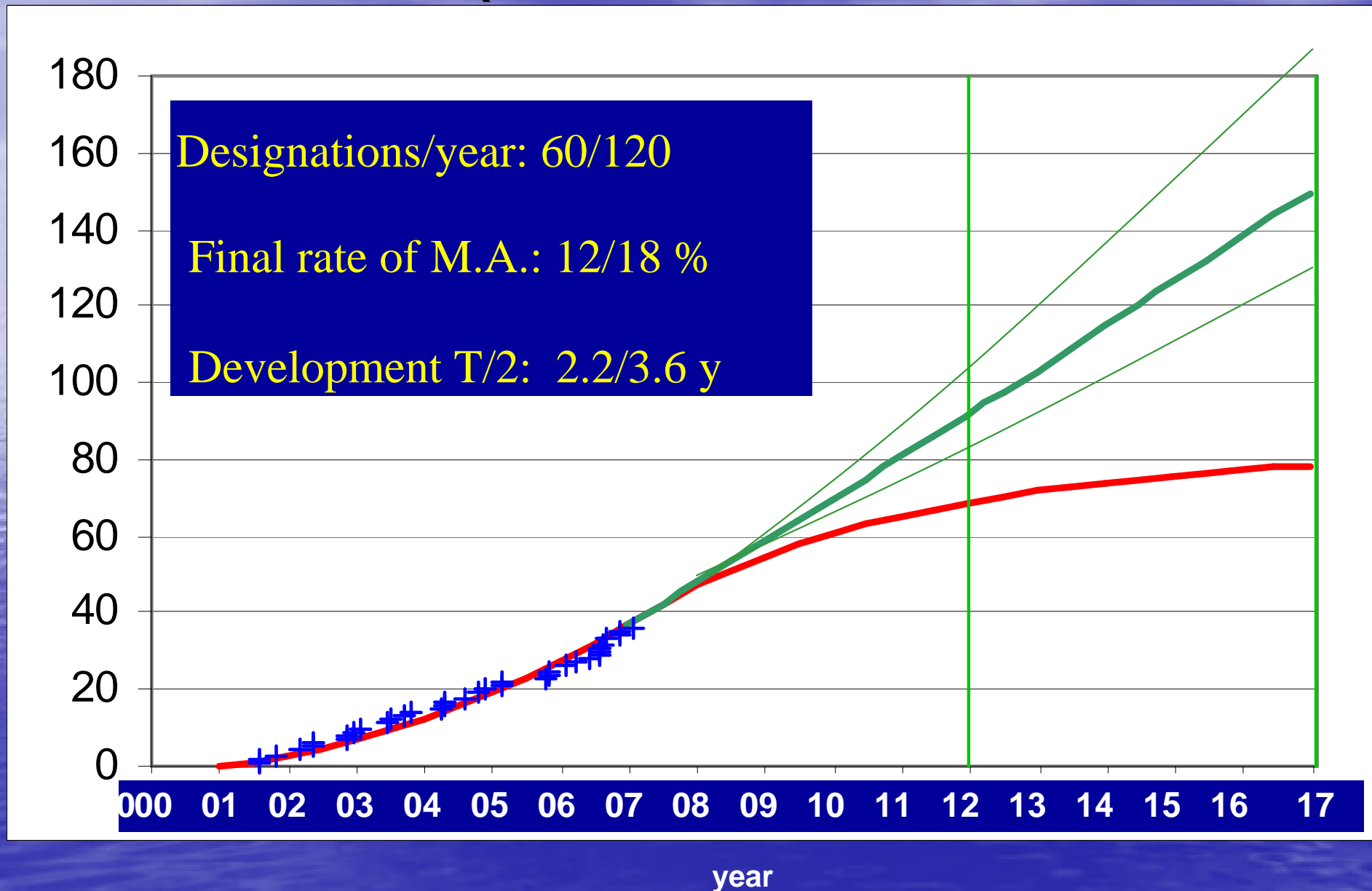
Distribution of opinions



Status of Orphan Marketing Authorisation Applications as of October 2007

-  42 Authorisations granted to date
-  3 CHMP Opinions in decision-making
-  12 Marketing Applications in EU review process
at CHMP/EMEA
-  1 Variation / Line Extension in review process:
-  22 Applications Withdrawn and 3 Negative
Decisions/Refusals

5 year forecast for possible approved orphan drugs (From Eurordis)



What's next – in drug development?

From "one drug fits all" blockbuster model –
towards targeted treatment solutions for patients
within particular diseases

- Innovative medicines/advanced therapies/targeted/personalised medicines
- Orphan Diseases/Orphan Drugs as models
- Collaboration between different companies and academic groups

Orphan Designated Gene Therapy Products for:

- **Duchenne's muscular dystrophy, calpainopathy, gamma sarcoglycanopathy, lipoprotein lipase deficiency, congenital alpha-1 antitrypsin deficiency, glycogen storage disease type II (Pompe's disease), Leber's congenital amaurosis**
(Adeno-associated viral vectors)
- **Li Fraumeni Syndrome**
(Adenoviral vector containing the human p53 gene)
- **Severe Combined Immunodeficiency (SCID), SCID due to adenosine deaminase (ADA) deficiency**
(Retroviral vectors)
- **Metachromatic leucodystrophy, Wiskott-Aldrich syndrome**
(Lentiviral vectors)

Orphan Designated Gene Therapy Products

(for cancer a.a. antisense products excluded)

- Adenovirus-Interferon gamma-coding DNA sequence for **cutaneous T-cell lymphoma**
- Adenovirus-mediated Herpes Simplex Virus-thymidine kinase gene for **high-grade glioma** with subsequent use of ganciclovir sodium
- Genetically modified allogeneic (human) tumour cells for the expression of IL-7, GM-CSF, CD80, and CD154 in fixed combination with a DNA-based double stem loop immunomodulator (dSLIM) for **renal cell carcinoma**
- Herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes as adjunctive treatment in **haematopoietic cell transplantation**
- Vascular endothelial growth factor-D gene in an adenoviral vector for use with a collagen collar for **prevention of stenosis in synthetic grafts used in haemodialysis**
- Herpes simplex virus lacking infected cell protein 34.5 for **glioma** (not gene therapy in the regulatory sense)

Cell and tissue therapies with orphan designation

- Human autologous mesenchymal adult stem cells extracted from adipose tissue for treatment of **anal fistula**
- Human heterologous liver cells (for infusion) for treatment of **acute liver failure**
- Human heterologous liver cells (for infusion) for treatment of **ornithine-transcarbamylase deficiency**
- Bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogenic) embedded in a plasma matrix for treatment of **epidermolysis bullosa**

What's on?/What's next?

- **Economics:** Increase in jobs/SMEs, increase in R&D expenditure
 - **Transatlantic collaboration:**
 - EMEA/FDA - Parallel Protocol Assistance/Scientific Advice
 - COMMON EMEA/FDA APPLICATION FORM for orphan medicinal product designation

Harmonisation of grounds for designation?

Potential for Global Collaboration - Japan? Australia?
 - **Research grants:** FP 5-6 support RDs/SMEs; FP7 (2007-13): RDs "FP7 priority"; Support for clinical trials ph. I-II in designated orphan drugs (2009)
- Future expansion? EU Commission to use COMP members as experts ?*

What's on/What's next?

- Increasing role of COMP visavi stakeholders (patient organisations, industry, health care professionals/academia) – "meeting point"
- COMP members in Scientific Advice Working Party Scientific Advice/Protocol Assistance – "full" members
- COMP members as observers in Paediatrics Committee (PDCO)
- COMP member in EU Commission Rare Disease Task Force
- COMP as advisors to the EU Commission (DG Enterprise/Sanco/Research)
- COMP members as Member States "ambassadeurs" for Rare Diseases/Orphan Drugs

Opportunities

- Potential benefits for 15 milj. European patients with rare conditions
- Potential benefits for neglected diseases (tbc, malaria etc.) – rare in the EU – prevalent in the rest of the world
- Potential benefits for common conditions! – learn from the rare (William Harvey)

Challenges

Profitability – Costs - Availability