



5th European Conference on Rare Diseases, Krakow

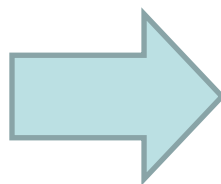
10 years of experience with Orphan drugs and
challenges for the future

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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”;...such action is best taken at Community level in order to take advantage of the widest possible market and to avoid the dispersion of limited sources...”

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”

Which incentives in the EU for Orphan Drugs?

- **Economic / Marketing**

- Reduction / Exemption fees

- (Extended incentives for SMEs - post authorisation)

- **Market Exclusivity** in the EU 10 years (+2)

- **Product development**

- Protocol assistance (Free scientific advice on drug development - linked to success in marketing authorisation)

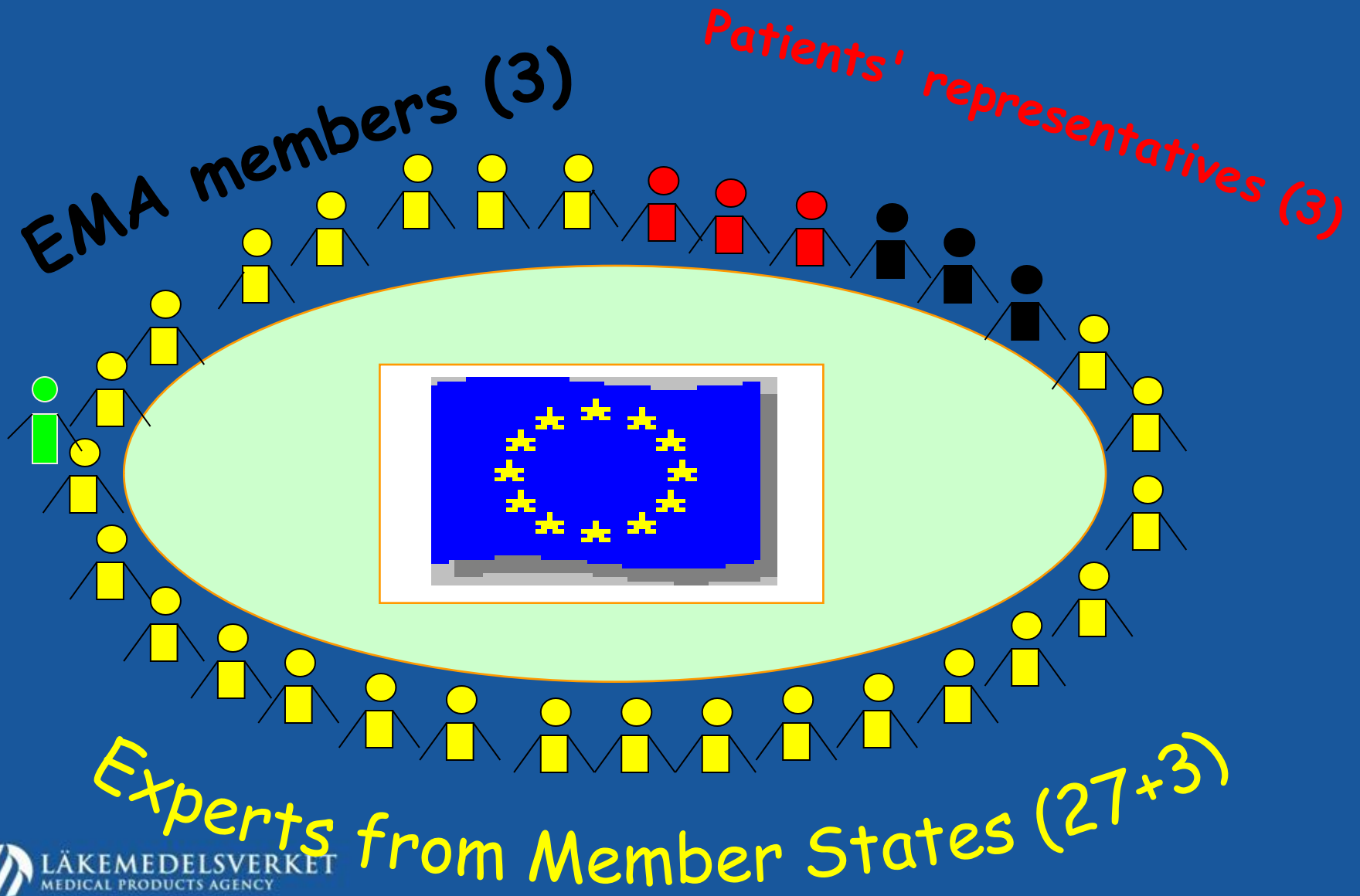
- **Community marketing authorisation**

- **National incentives** (EC inventory)

- **Priority to EU Research - Framework programs**

- **e.g.** clinical trial grants, 2009

Committee for Orphan MP's (COMP)



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

Orphan designation, criteria

- **RARITY (prevalence)**

Medical condition affecting not more than 5 in 10,000 persons in the Community (around 250,000)

OR

- **NON RETURN on INVESTMENT**

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 condition

- **ALTERNATIVE METHODS AUTHORISED**

- If satisfactory methods exist, the sponsor should establish that the product will be of **significant benefit** for those suffering from the condition

10 years of the Orphan Regulation in Europe conference - The experience up to date

- > 1113 orphan designation applications
- > 724 orphan designations, more than 1/3 affect less than 1 in 10,000 in the EU. Around 30% of designations - innovative products
- Few negative opinions/year/Withdrawals may reapply at a later stage
- 62 marketing authorisations (40% with prevalence < 1/10,000)
- **Public Health Impact – General:** drugs for children and for diseases rare in the EU (e.g. tropical diseases)
Public Health Impact – Examples: More than 1/3 of authorised ODs for rare cancers followed by lysosomal storage diseases)

COMP 10 year outcome (cont.)

➤ COMP advisory role to the EU Commission (examples)

DG Research: e.g. Preclinical models, Grants for preclinical and clinical trials

- DG Sanco e.g. participation in Rare Disease Task Force, involvement in WHO ICD-11 revision procedure for rare Diseases

➤ COMP International collaboration (examples)

e.g. FDA/OOPD

- Common application form for orphan designation applications
- Common annual report on “Rare disease day” (optional)
- Regular teleconferences
- Parallel scientific advice/protocol assistance

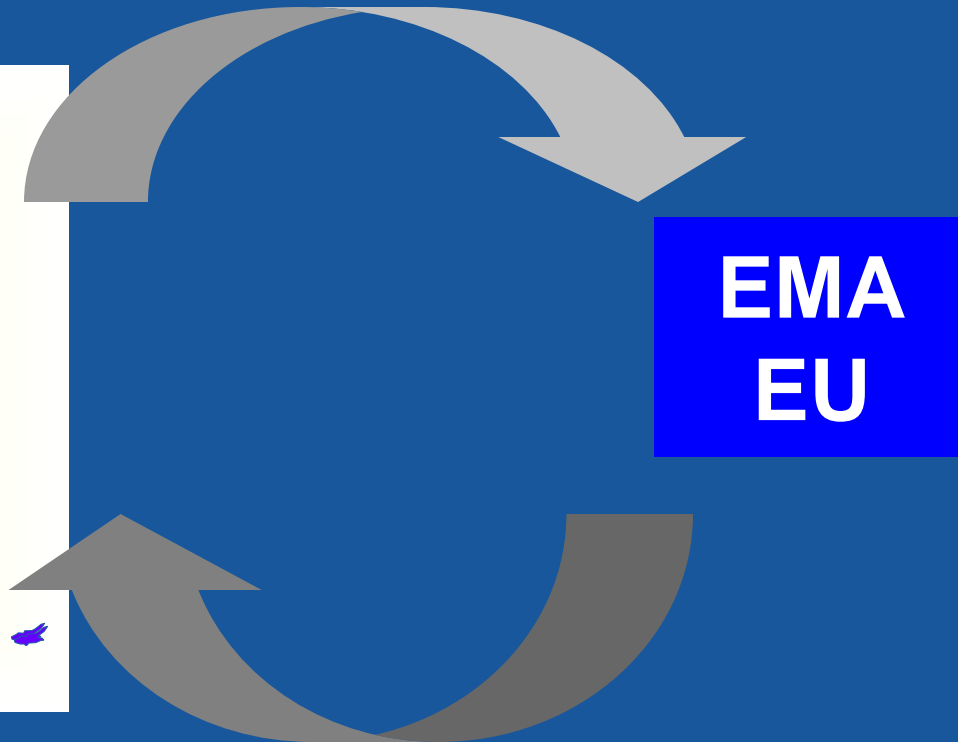
Orphan Drug Development in the EU - Before the Orphan Regulation - Stakeholders' situations

- Patients with serious rare conditions: A handful of authorised drugs available
- Industry: mostly 'big pharma' - mostly 'blockbuster development'
- Health Care Professionals/Academia: Virtually no involvement in drug development
- Regulators: 27 (at least) different procedures for marketing authorisation of new drugs

Orphan Drug Development in the EU – 10 years after the implementation of the Orphan Regulation - Stakeholders' situations

- Patients with serious rare conditions: > 700 orphan designated products; 62 orphan drugs centrally authorised
- Industry: 'Micro/Small/Medium-sized enterprise' expansion in orphan drug development; Small pharma developing into big pharma; Big pharma interest in orphan drug niches
- Health Care Professionals/Academia: represented among sponsors of orphan designation applications – some authorised
- Regulators: 1 procedure – centralised applications for marketing authorisation to the EMA, decision by EU commission

Europe – Before and Now



What is done by Member States in common today?

- **ODD**= Orphan Drug Designation: Committee for Orphan Medicinal Products, **COMP/EMA**
- **PA**= Protocol Assistance: Scientific Advice Working Party, **SAWP/CHMP/COMP/EMA**
- **PIP** = Paediatric Investigation Plan: Paediatrics Committee, **PDCO/EMA**
- **MAA** = Marketing Authorisation Application: Committee for Medicinal Products for Human Use, **CHMP/EMA**
 - Review of orphan designation criteria at MAA**COMP/EMA**
- **Post-MA** obligations, additional studies, follow-up registries assessed by **CHMP/EMA**

What is not done by Member States in common today?

- Decisions on Pricing & Reimbursement
- Assessment of the Clinical Added Value and/or other Health Technology Assessments

What's next – in orphan drug development? Opportunities

EU cooperation on Health Technology Assessment

- Objectives:

Avoid duplication of efforts/resources for industry/HTA bodies and national decision makers

Instruments (among others)

- Joint Action Member States /Commission on HTA 2010-2012
- Call for tender on assessment of clinical added value for orphan medicines

(As presented by Mr M Terberger, EC, DG Sanco, at 10 year anniversary conference of orphan regulation, EMA, May 3-4, 2010)

RDs/ODs in the EU - Challenges/Opportunities

Member States' level - EU/ International level

- Formulation and implementation of national plans/strategies on rare diseases; Identification of unmet medical needs
- Awareness raising: public, political, research policies/councils, patient organisations - "Non-discrimination act" common vs rare diseases
- Creation of, access to and coordination of centers of expertise, promoting rational treatment with orphan drugs
- Creation of follow-up systems for evaluation of treatment with orphan drugs in clinical practice, e.g. registers of orphan drugs for research, health care and authority use – supporting early and efficient introduction of new orphan drugs
- Adjustments of financial (reimbursement) systems to facilitate early introduction of and access to treatment with orphan drugs, e.g. conditional reimbursement
- Measures to stimulate and render more effective research – basic/translational; Interaction (academics, doctors, patients, industry) and networking, e.g. ERA-Net

What is/will be the role of the COMP?

- Increasing role of COMP visavi stakeholders (patient organisations, industry, health care professionals/academia) – "meeting point"
- COMP member in EU Commission Rare Disease Task Force – COMP chair/vice-chair observer in EUCERD
- Increasing importance of the COMP as advisor to the EU Commission (DG Enterprise/Sanco/Research)
- COMP members as Member States "ambassadors" for Rare Diseases/Orphan Drugs

EU Orphan Regulation 141/2000 - Opportunities for patients with rare conditions

- Potential benefits for > 30 milj. European patients with rare conditions
- Potential benefits for neglected diseases, rare in the EU – prevalent in the rest of the world
- Potential benefits as 'role model' - Orphan Regulation – COMP – for the development of drugs for common diseases; for EU collaboration in other areas/aspects of rare diseases



CONCLUSIONS

The Orphan regulation has been a success!

THANKS TO:

Patient Organisations
and EU collaboration

