Fourth European Healthcare Policy Deciders Forum

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Member States Perspective: Sweden

Kerstin Westermark

Senior expert, Medical Products Agency, MPA

Chair, Committee for Orphan Medicinal Products, COMP, EMA

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Orphan drugs and effectiveness
Why important to study?

CHARACTERISTICS OF RARE DISEASES

A rare disease in Europe is a disease affecting not more than 5 in 10,000 citizens

- Many are of genetic origin
- 50% affect children
- 5,000 to 8,000 distinct rare diseases
- 6 to 8 % of the EU population affected over lifespan
- 27-36 million people affected in the EU
- Serious, chronic and often life-threatening
- Patients are few and geographically spread
- Relevant information is scarce
- Experts are few
- Resources are limited
- Research is fragmented

www.eurordis.org

EURORDIS
Rare Diseases Europe

Orphan designation, criteria

- **RARITY (PREVALENCE)**
  Not more than 5 in 10,000 persons in the Community
  OR
  NON RETURN on INVESTMENT

- **SERIOUSNESS**
  Life - threatening or chronically debilitating condition

- **ALTERNATIVE METHODS AUTHORISED**
  - If satisfactory methods exist, the product must be of **significant benefit** for those suffering from the condition

Orphan drugs and effectiveness Why important to study?

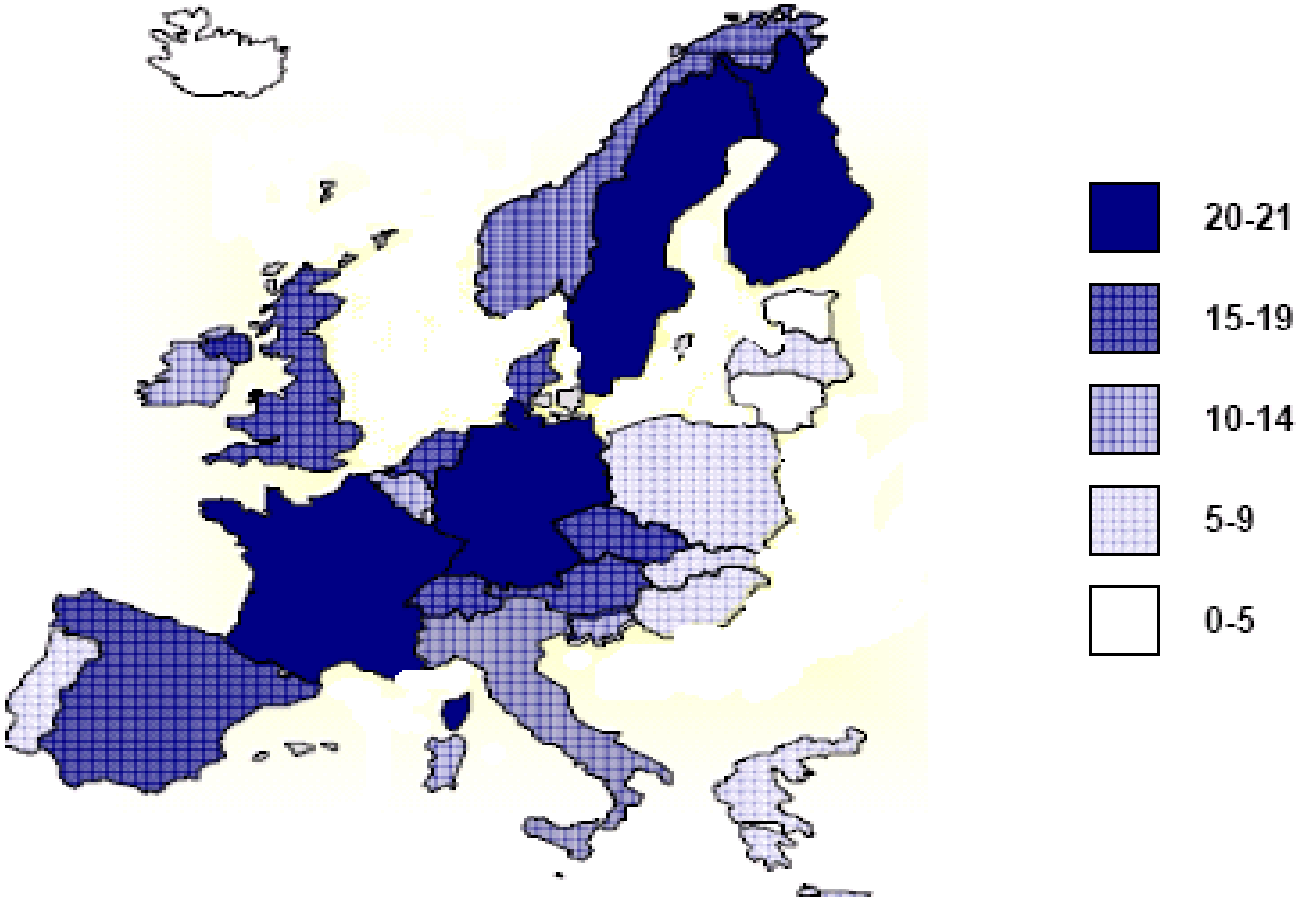
2000-2010: 63 Marketing Authorizations for Orphan drugs

Marketing authorisation procedures:

- 24/63 (38%) Under exceptional circumstances
  - Comprehensive data can normally never be provided because indication too rare
- 4/63 (6%) Conditional approvals
  - Further clinical data to confirm benefit-risk balance
- 35/63 (56%) Normal approvals
  - Comprehensive data to assess risk-benefit balance

Limited data available at the time of Marketing authorisation

Numbers of orphan drugs available in EU markets in 2006



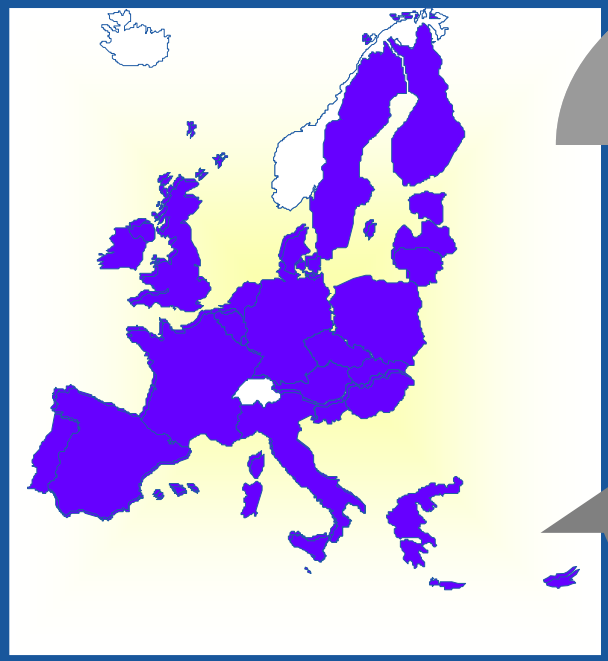
**Source: Eurordis (2007) (Eurordis survey on orphan drugs)*

EU communications and recommendations on rare diseases and orphan drugs

- **Conclusions and Recommendations from the High Level Pharmaceutical Forum** (adopted November, 2008)
  "Improving Access to orphan medicines for all affected EU citizens"
  http://europa.eu/pharmaforum/docs/final_conclusions_en.pdf
- **Commission Communication and Recommendation on Rare Diseases; "Rare diseases - Europe's challenges"**
  (adopted December 2008)
  http://ec.europa.eu/health/ph_threats/non_com/rare_10_en.htm
- **COUNCIL RECOMMENDATION of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02)** (national plans/strategies; centres of expertise; EU collaboration; patient empowerment) (adopted June 2009)
  http://ec.europa.eu/health/ph_threats/non_com/docs/rare_rec_en.pdf

European Union – Before and Today

From 27 different procedures for marketing authorisation - to 1 procedure for 27 Member States



EMA
EU

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What is done by Member States in common today?

- Orphan Drug Designation
- Protocol Assistance
- Paediatric Investigation Plan
- Marketing Authorisation (MA) including Review of orphan designation criteria at the time of MA application
- Post-MA obligations, additional studies, follow-up registries

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What is not done by Member States in common today?

- Assessment of Clincal Added Value (CAV)
- Health Economic Assessments
- Pricing & Reimbursement

EU has > 33 different pricing/reimbursement systems

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Assessment of effectiveness/relative effectiveness? Opportunities for EU collaboration

EMA level – at the time of marketing authorisation:

- EMA/EUnetHTA collaboration (CHMP: European Public Assessment report, EPAR improvement)

  COMP: Public versions of Review of Orphan Designation criteria , 'significant benefit'

- 'CAVOD': Feasibility study ongoing on creation of a mechanism for exchange of knowledge between MS and European authorities on the scientific assessment of the clinical added value for orphan medicines (Ernst&Young)

'The Swedish effectiveness project ' – postmarketing

Drug effectiveness – what do we mean?

Definitions according to High Level Pharmaceutical Forum

- **Efficacy:** is the extent to which an intervention does more good than harm under ideal circumstances

- **Effectiveness:** is the extent to which an intervention does more **good** than **harm** when provided under the usual circumstances of health care practice

- **Relative effectiveness:** is the extent to which an intervention does more good than harm compared to one or more intervention alternatives when provided under the usual circumstances of health care practice

Conclusions from the Swedish EU Presidency conference

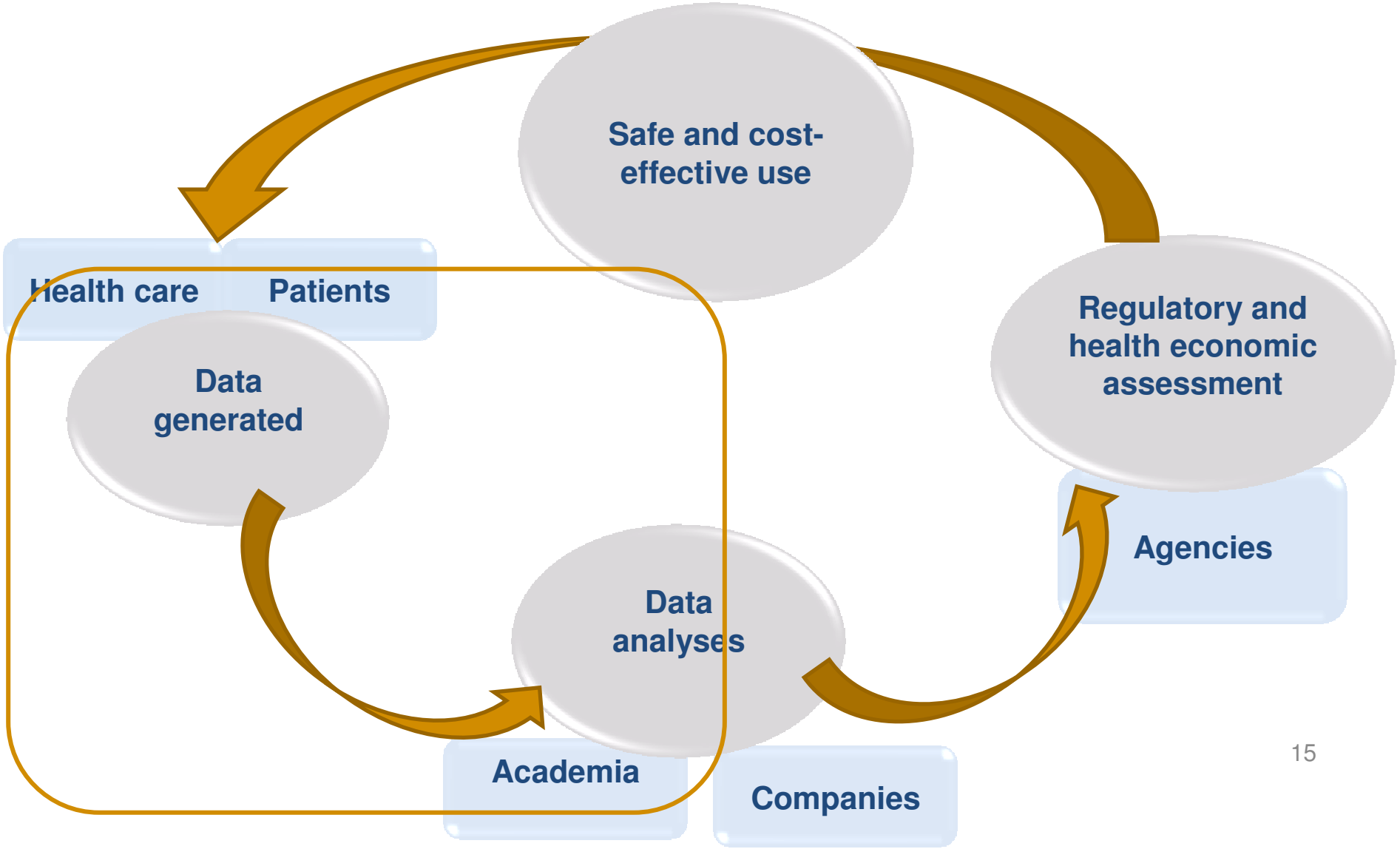
- Agreement on the need for data on drug efficacy, safety and cost-effectiveness in clinical practice
- Orphan diseases, rare outcomes – multinational data collection needed
- Approriate models for pricing and reimbursement may improve post-approval study design
- Expanding cooperation between European HTA agencies
- The importance of co-morbidity and co-medication data in the assessment of drug effectiveness was highlighted
- Further exploration of the field by a pilot project was supported– key stakeholders *(European Commission, EMA, EUnetHTA, EFPIA, National Competent Authorities, Patient organisations)* prepared to contribute

Aims of the project as stated by the Oversight Committee

- "Explore methodological challenges relating to multinational collection and sharing of data relevant to the assessment of drug effectiveness."

- "Identify solutions used by existing clinical networks to meet these challenges and thereby, facilitate the development of working procedures and datasets that may be useful for patient care and agency assessment as well as for research and industry needs at the national and European level."

Limitation of projects scope to generation, collection and sharing of data



Limitation of scope by selection of disease areas

- **Cancer** – severe diseases, many new drugs often orphan disases, substantial economic impact
- **Chronic inflammation** – many new biologics with unknown long-term effects, Nordic registry experience
- **Orphan diseases**– few patients, small data sets, requires multinational data collection

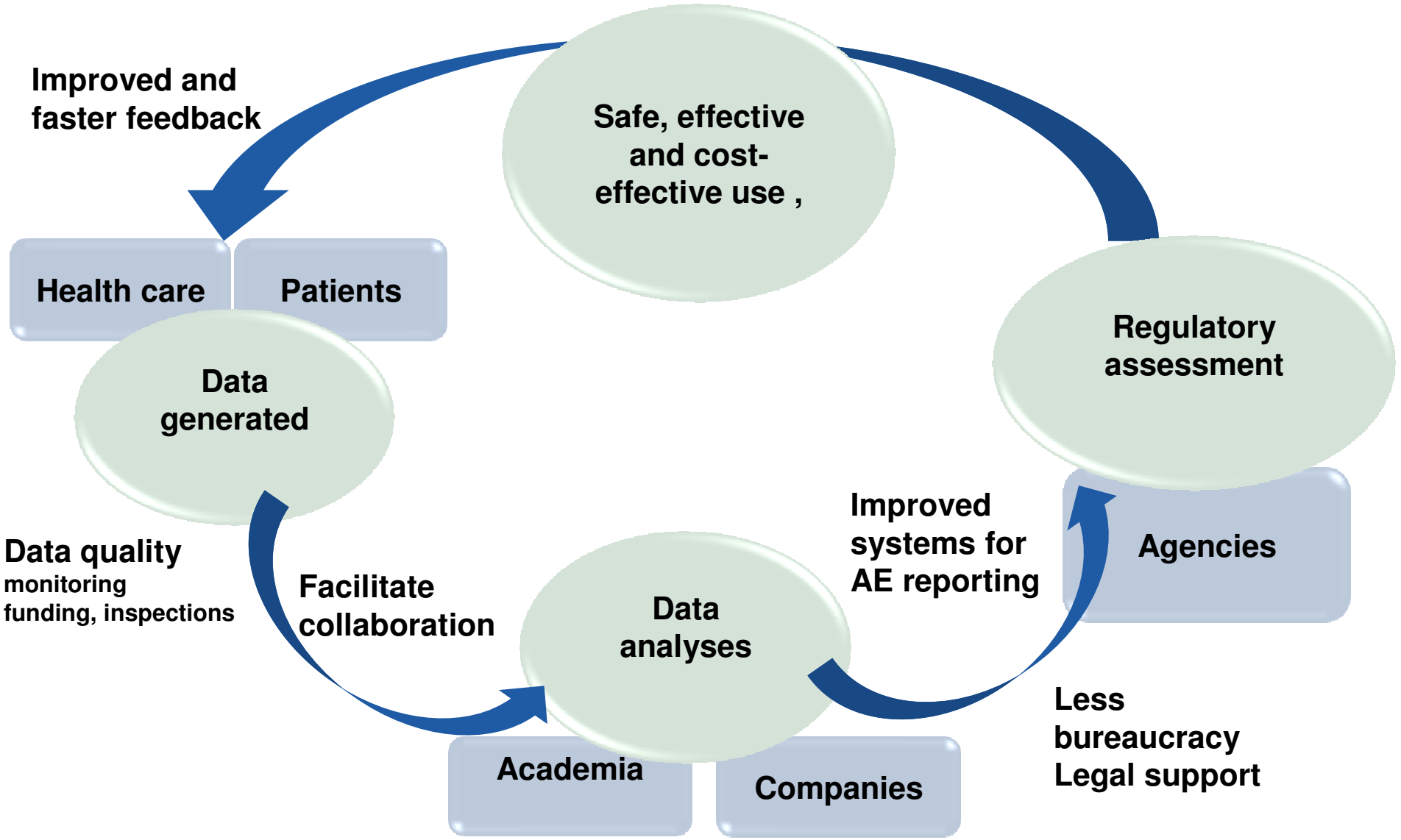
Network candidates chosen by applying feasibility and relevance criteria

- Therapeutic area with recently approved drugs and effectiveness issues requiering multi-national data collection
- Well functioning clinical network within the EU
- Transparent financing
- Willingness to share data
- Potential health economic impact
- Varying availability with the EU
- Widespread off-label use
- Potential to stimulate methodological development and drug innovation

Networks/registers expressing interest to participate

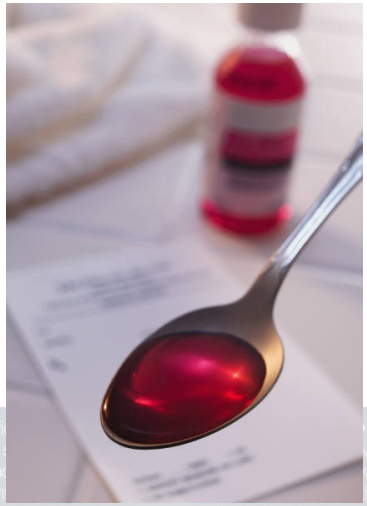
- Cryopirin-associerade syndromes (CAPS)
- DANBIO – Danish Biologics Rheumatology Register
- EUTOS – Chronic myeloid leukemia (CML)
- Multiple sclerosis-register
- SCOT study
- Velcade

Identified Areas for Improvement



What to do next in the SPADE project?

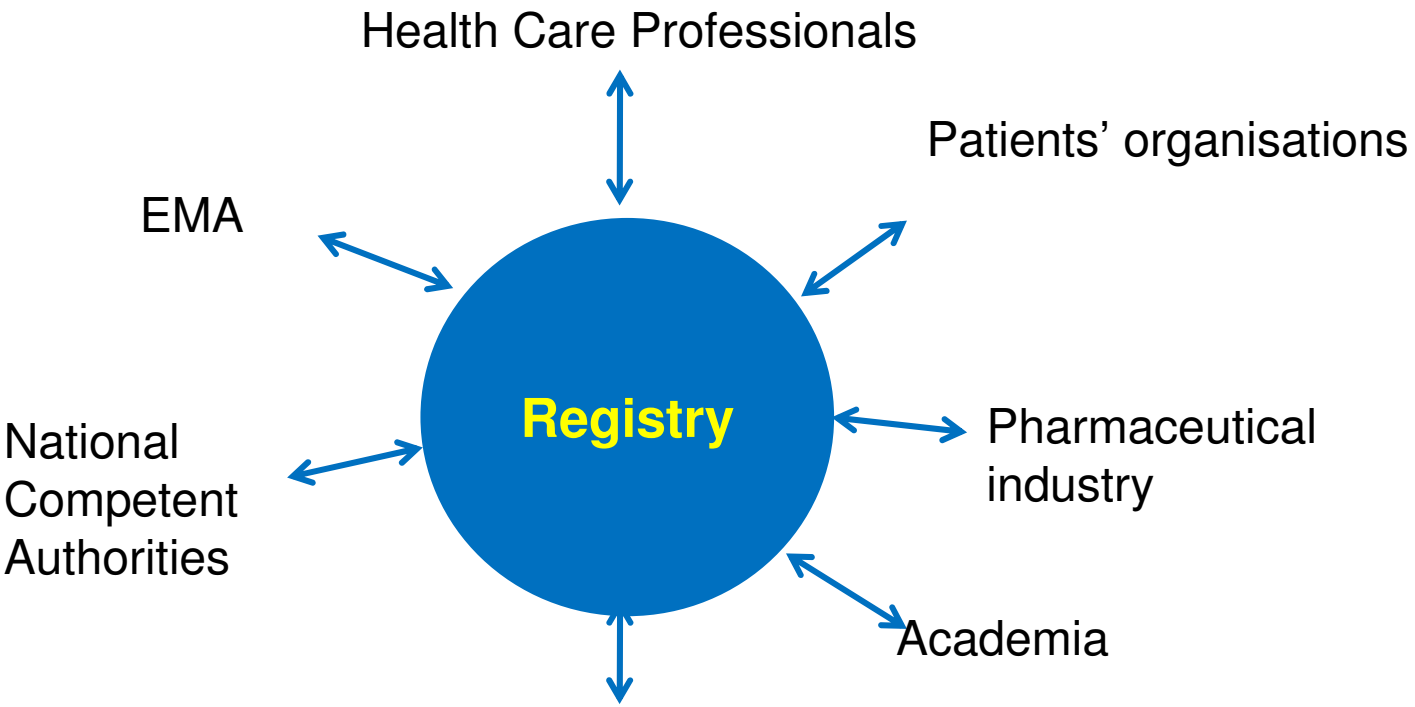
- In depth analyses of data/complementary information collection
- Perform ethics/legal and management substudies (Hansson and Helgesson)
- Define the most important problem areas
- Propose actions to support improvement efforts by registers/network



Conclusions I
Opportunities of EU-collaboration –
The Swedish effectiveness project as an example

- Improvement of follow-up systems ’Best practise registry guidance’, ’Good Registry Practise´
- Stakeholders gather around one registry rather than one registry/stakeholder
- Publically (hospital) owned data - available at cost prize

One registry - many stakeholders



Conclusions II

Making orphan drugs accessible for patients in a timely manner - the way forward?

- Create EU follow-up systems for orphan drugs - to support early and rational introduction of orphan drugs
- Create EU-wide networks based on national centers for rare diseases to allow for early and efficient treatment with orphan drugs
- Financing

  a) at EU-level to support infrastructures/reigistries

  b) at national level to facilitate early introduction of treatment with orphan drugs

  Best way to give rapid access to treatment, while collecting large amount of patient data, allowing for rapid decision on value for money - without withholding treatment from patients

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CONCLUSIONS

Success factor:
EU collaboration

Back-up slides

Orphan Regulations in the EU

- 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

"Persons suffering from rare conditions should be entitled to the same quality of treatment as other patients; it is therefore necessary to stimulate the development…;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"

EU Incentives
Orphan Designated Medicinal Products

- **Economic / Marketing**

  - Reduction / Exemption fees

  (Extended incentives for Small and Medium-sized Enterprises post authorisation)

  - Market Exclusivity 10 years in the EU
- **Product development**

  - Protocol assistance (= Scientific advice for orphan drugs)
- **Community marketing authorisation**
- **National incentives** (EC inventory)
- **Priority to EU Research - Framework programs**