The Implementation of the EU Orphan Regulation -

What has changed for drug development?

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”Learning from the Rare”

“…Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature by the careful investigation of cases of rarer forms of disease”.

(Letter by William Harvey, year 1657)


Finland
Sweden
Estonia
Latvia
Lithuania
Denmark
Ireland
United Kingdom
Netherlands
Belgium
Germany
Luxembourg
Poland
Czech Rep.
Slovakia
France
Austria
Slovenia
Hungary
Romania
Bulgaria
Italy
Spain
Portugal
Greece
Malta
Cyprus

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"

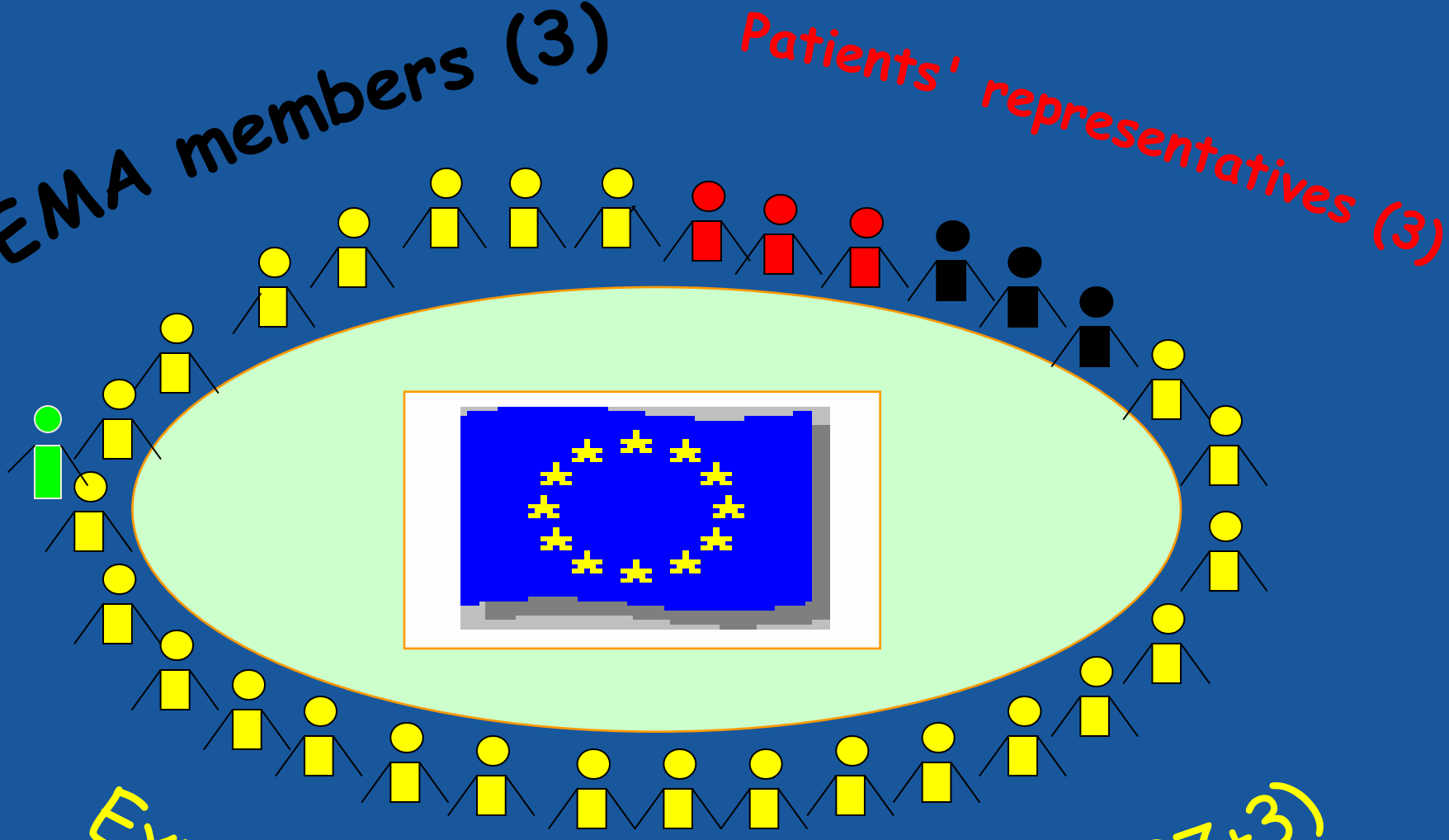
As…

"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 (OMP)

- **Economic / Marketing**
  - Reduction / Exemption fees
    (Extended incentives for SMEs - post authorisation)
  - Market Exclusivity in the EU 10 years (+2)
- **Product development**
  - Protocol assistance
- **Community marketing authorisation**
- **National incentives** (EC inventory)
- **Priority to EU Research - Framework programs**
  - **e.g.** clinical trial grants, 2009

Committee for Orphan MPs (COMP)



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Tasks of the COMP

- Examine applications for designation of a medicinal product as an orphan medicinal product (OMP)
- Assist the Commission in drawing up guidelines
- Assist the Commission in liaising internationally and with patient support groups
- Advise the Commission on a policy on orphan medicinal products for the EU

COMP particularities

- First EMA committee to have patients' representatives as full members
- The only EMA Committee lacking alternate members
- COMP members: around 50% from national medicines agencies – around 50% from academia/health care professionals
- Orphan designation applications free of charge - No compensation for Member States

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

…the level of evidence…

CHMP

COMP

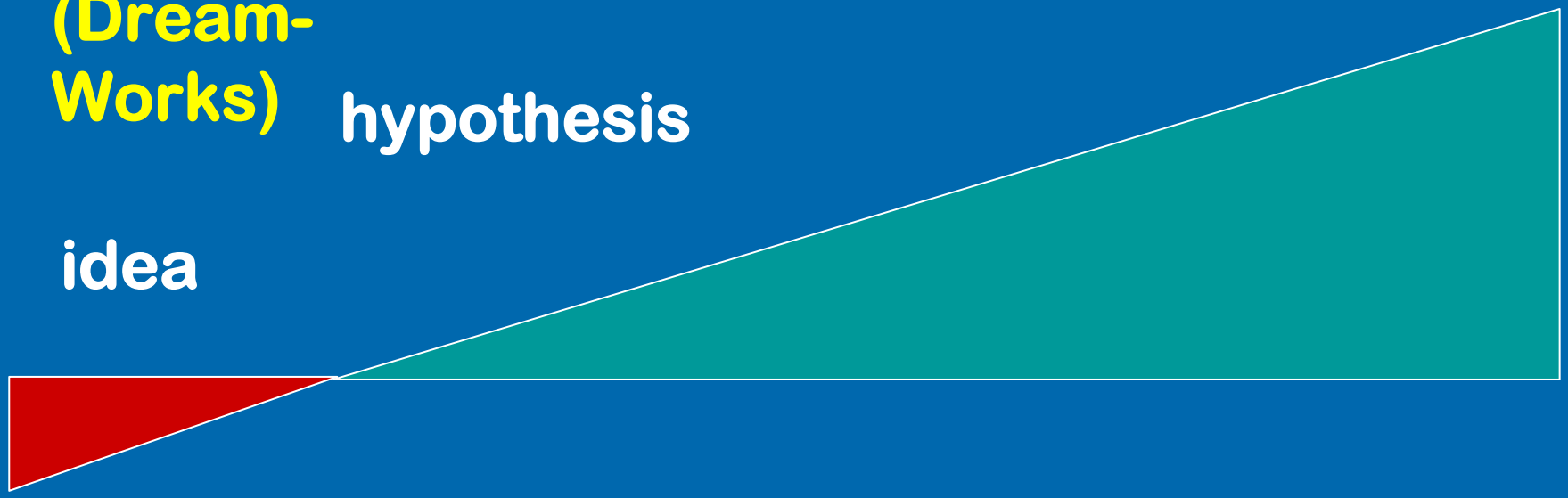
evidence

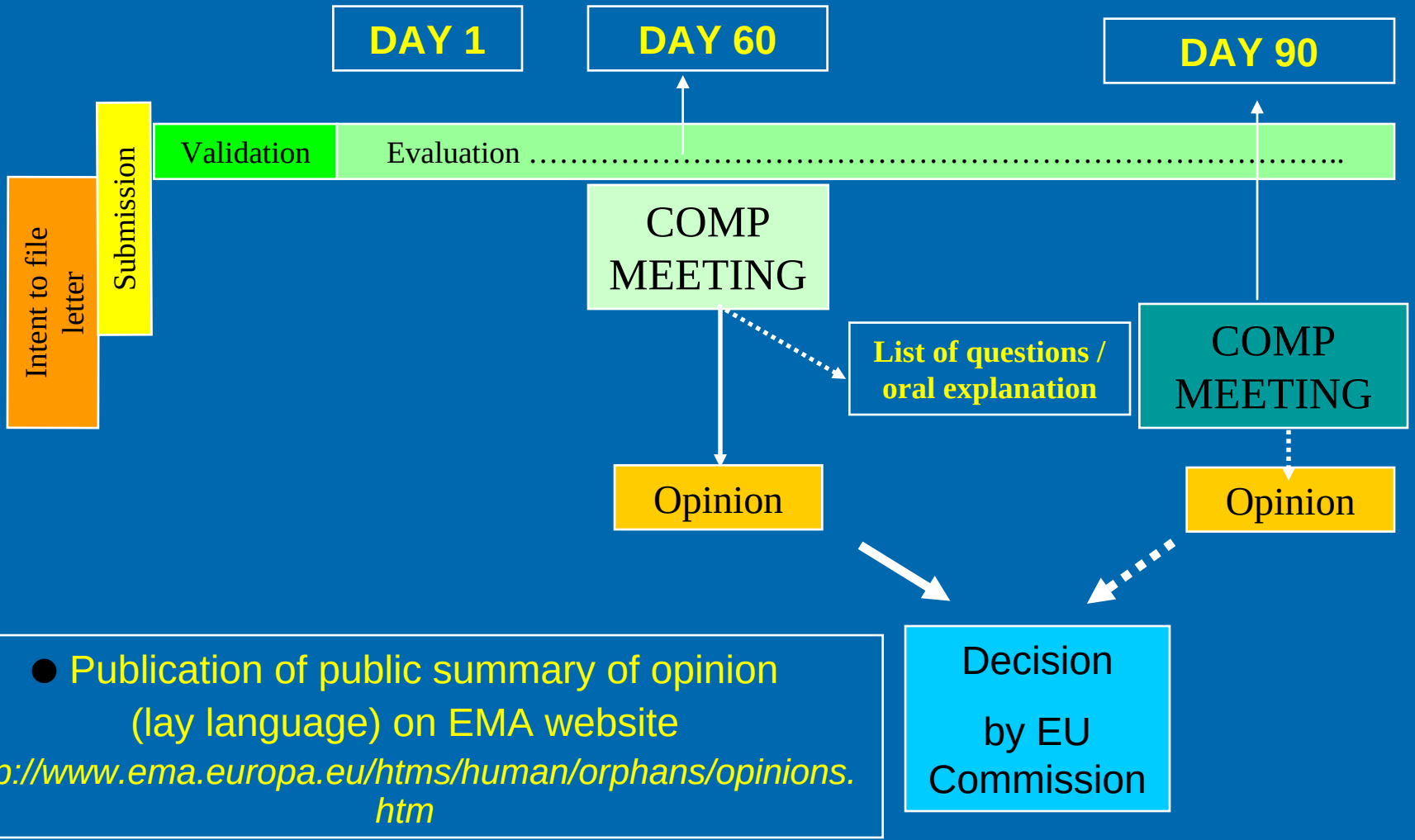
plausible
assumption

(Dream-
Works)

hypothesis

idea





- Publication of public summary of opinion (lay language) on EMA website *http://www.ema.europa.eu/htms/human/orphans/opinions.htm*

COMP 10 year outcome

- > 1000 orphan designation applications
- > 700 orphan designations: c:a 30% innovative products (fusion proteins, monoclonal antibodies, oligonucleotides), 7% advanced therapies (cell/gene/tissue)
- 60 marketing authorisations (41% with prevalence < 1/10,000), 41% ‘under exceptional circumstances’; 5% ‘conditional approval’
- Public Health Impact – General: drugs for children and for diseases rare in the EU (e.g. tropical diseases)

  Public Health Impact – Examples: 1/3 of authorised ODS for rare cancers (e.g. Tyrosine kinase inihibitors for chronic myeloid leukaemia; Endothelin receptor antagonists for pulmonary arterial hypertension; Enzyme replacement therapies for 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: 60 orphan drugs centrally authorised

  > 700 orphan designated products

- Industry: Mostly 'small pharma' – around 2/3 of orphan designated products;

- 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

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 – EU collaboration in other areas/aspects of rare diseases

CONCLUSIONS

The Orphan regulation has been a success!

THANKS TO:

Patient Organisations

EU collaboration