EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Orphan designation
Key concepts and evaluation criteria

Workshop for Micro, Small and Medium-sized Enterprises

Focus on scientific and regulatory advice

Presented by: Jordi Llinares
Head of orphan medicines

Outline

Overview orphan designation

Procedure and criteria

- Definition of a medical entity
- Significant benefit

Outcomes

Other activities

- Transparency

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Why an orphan regulation?

Rare diseases → developing and marketing cost would not be recovered by the expected sales

Persons suffering from rare conditions deserve same quality of treatment as other patients

Pharmaceutical industry does not develop medicines for rare diseases under normal market conditions

Objective of the Regulation

- provide incentives that stimulate research and development (push)
- modify market conditions (pull)
- Set up system of recognition orphan drugs entitled for incentives

Legal references in the EU

Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products of 16 December 1999

- Criteria for designation
- Committee (COMP)
- Procedure
- Incentives

Commission Regulation (EC) No 847/2000 of 27 April 2000

Commission communication July 2003 (2003/C 178/02)

Commission communication on Art 8(1) and (3) (C(2008) 4077)

Main characteristics orphan designation

For medicinal products for human use

Procedure free of charge

Can be requested at any stage of development

Sponsor can be either company or individual

- Established in the Community (EU, Ice, Liech, Nor)

European Commission Decision gives access to incentives

Incentives (I)

Fee reduction / exemptions

- Extended incentives for SMEs !

➔free protocol assistance

➔free marketing authorisation application

➔free post authorisation application and annual fee during first year from authorisation

Incentives (II)

10-year market exclusivity (+ 2 if paediatric)

- Protection from
  - similar products
    - Molecular structure
    - mech of action
    - for same indication
  - Three derogations (➔access to market even if similar)
    - Sponsor's consent
    - Lack of supply
    - Clinical superiority

Incentives (III)

- Protocol assistance
- Community marketing authorisation
- National incentives (EC inventory)

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Designation criteria

RARITY (prevalence) / RETURN OF INVESTMENT

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

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

ALTERNATIVE METHODS AUTHORISED

If satisfactory method exist the sponsor should establish that the product will be of significant benefit

Committee for Orphan Medicines (COMP)

- 1 elected Chair (Prof Kerstin Westermark)
- 1 Representative per Member State
- 3 Patients' Representatives appointed by Eur Commission
- 3 Members appointed by Eur Commission on proposal from Agency
- 1 Member for Norway, and 1 for Iceland

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Medical condition

EC Guideline (ENTR/6283/00)

- Any deviation(s) from the normal structure or function of the body, as manifested by a characteristic set of signs and symptoms (typically a recognised distinct disease or a syndrome)

Examples:

Duchenne muscular dystrophy

Gaucher disease

Mesothelioma

Additional considerations on the condition

- Development plausible based on pathogenesis and pharmacodynamics
- Distinct entity if: pathophysiology, histology, clinic presentation

E.g.

- Different severities- stages not acceptable

Second line treatment of …

Patients refractory to …

Acceptable subset .. exceptionally

Medically plausible subset:

Usually defined by characteristics of the drug that **limit the use** of the investigational medicinal product in only the subset of the patients with the disease:

- Subset is medically recognizable
- Drug **will not** be effective/safe for the rest of patients population not included in the subset

Subset example

Treatment of rhodopsin-linked retinitis pigmentosa

- *Subset is medically recognizable*
  - Retinitis pigmentosa is a group of hereditary diseases of the eye that lead to progressive loss of sight
  - Patients with rhodopsin-linked retinitis pigmentosa have a mutation in the gene for this protein

- *Drug **will not** be effective/safe for the rest of patients population not included in the subset*
  - *Product aims at providing a* normal copy of the rhodopsin gene

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Significant benefit

Definition:

"A clinically relevant advantage or a major contribution to patient care"

- Based on assumptions at the time of orphan designation
- Over authorised products (=satisfactory methods)
- Sign benefit to be confirmed prior to marketing authorisation to maintain orphan status
- Recommendation document on data for SB and plausibility

Examples assumption for significant benefit

Drug has a new mechanism of action leading to

- Better effect and potentially efficacy (to be demonstrated)
- Opens possibilities for drug combination and broadens therapeutic alternatives

More convenient administration route (major contribution to patient care)

- when documented problems exist with existing route

Complementary safety profile

- Weak assumption for justification of sign benefit (data to support?)

More on significant benefit

Higher level of evidence required at time of marketing authorisation compared to time of designation (in line with stage of development)

Comparative data may be necessary

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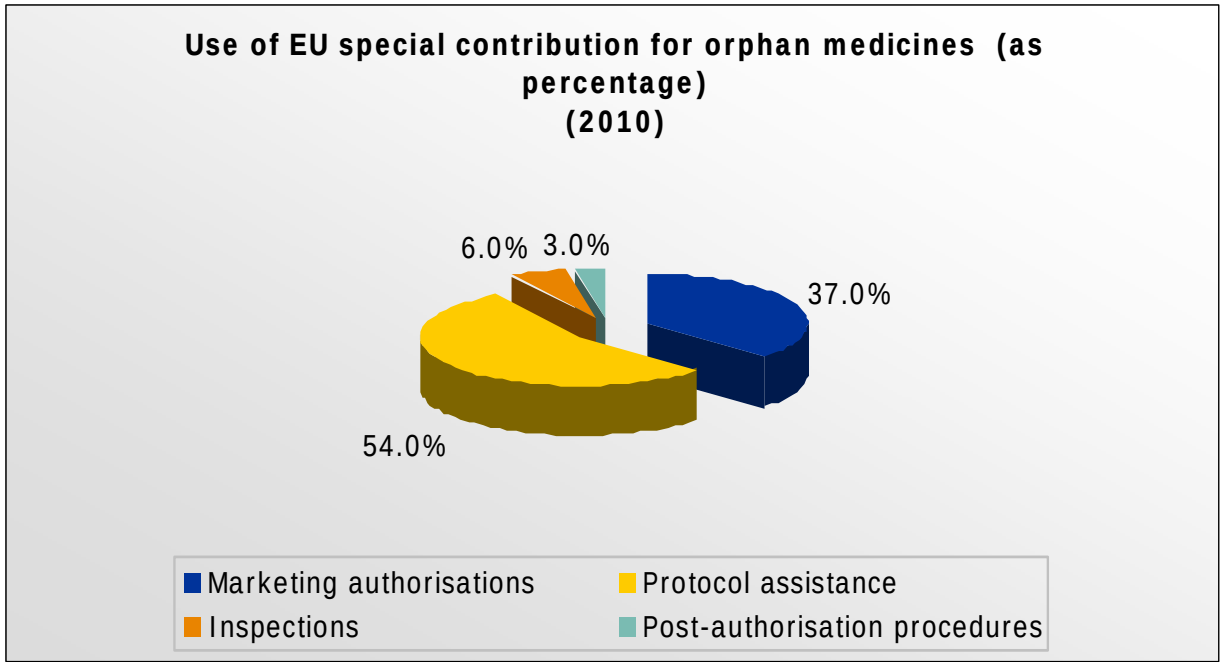
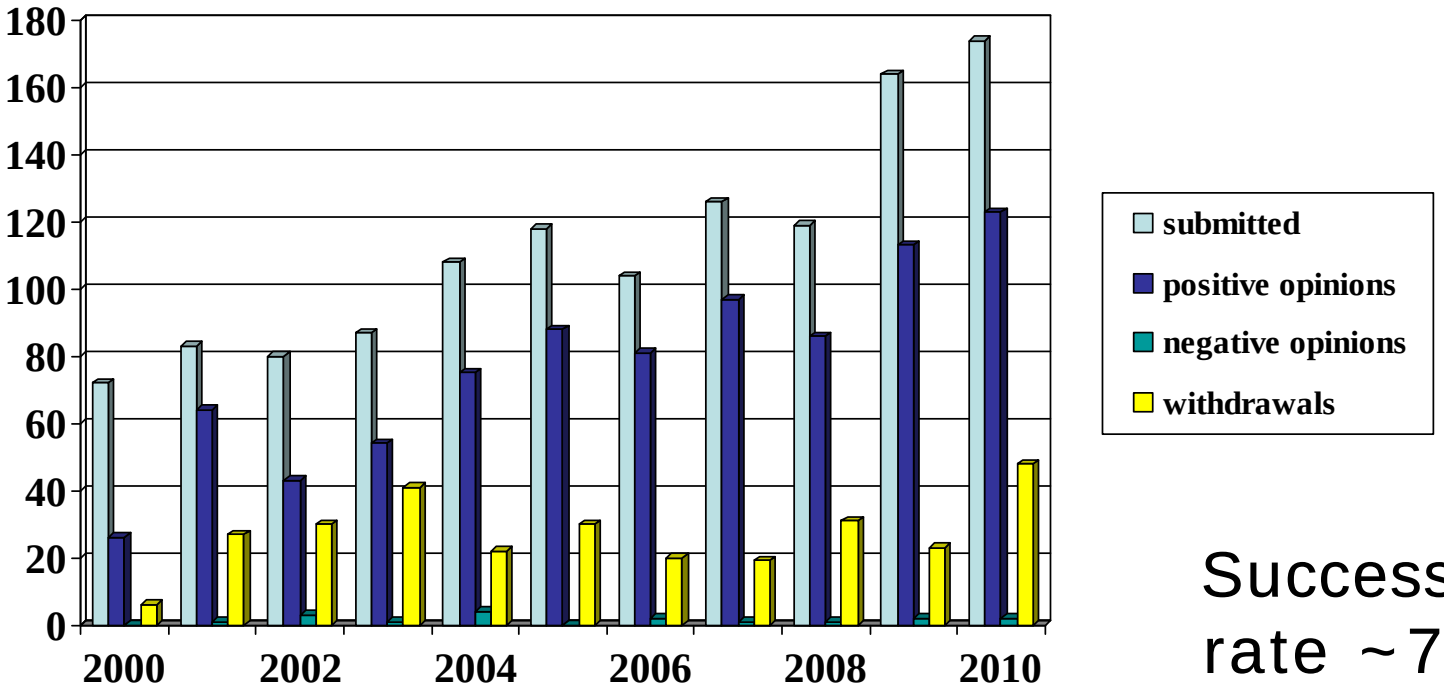
Use of incentives (EU contribution)



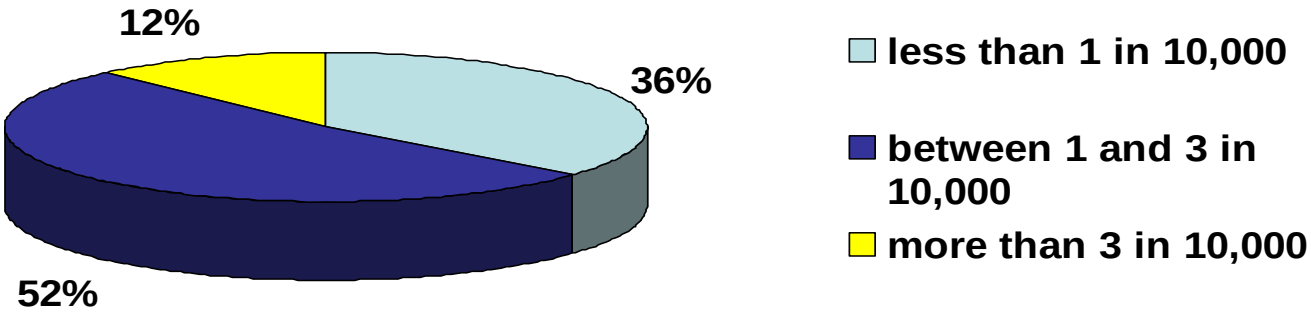
Approximately use of 6 million Euro per year

Outcome on designations

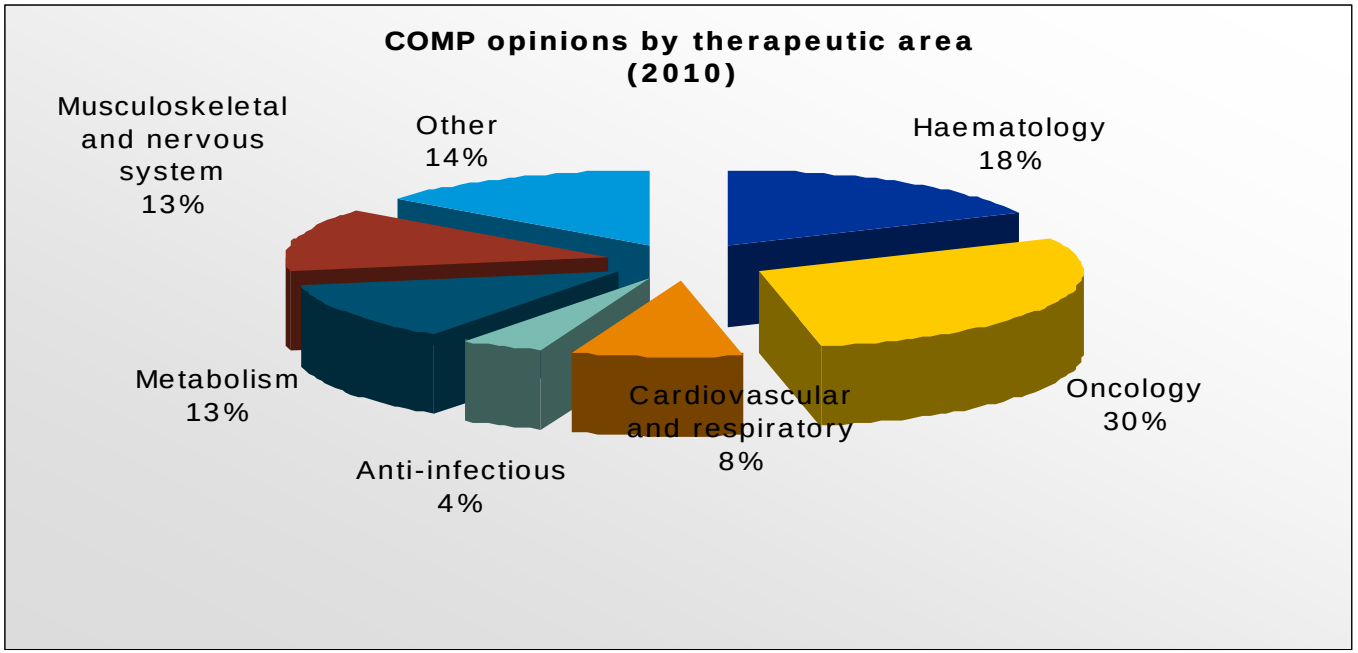


Success rate ~70%

Designations per prevalence



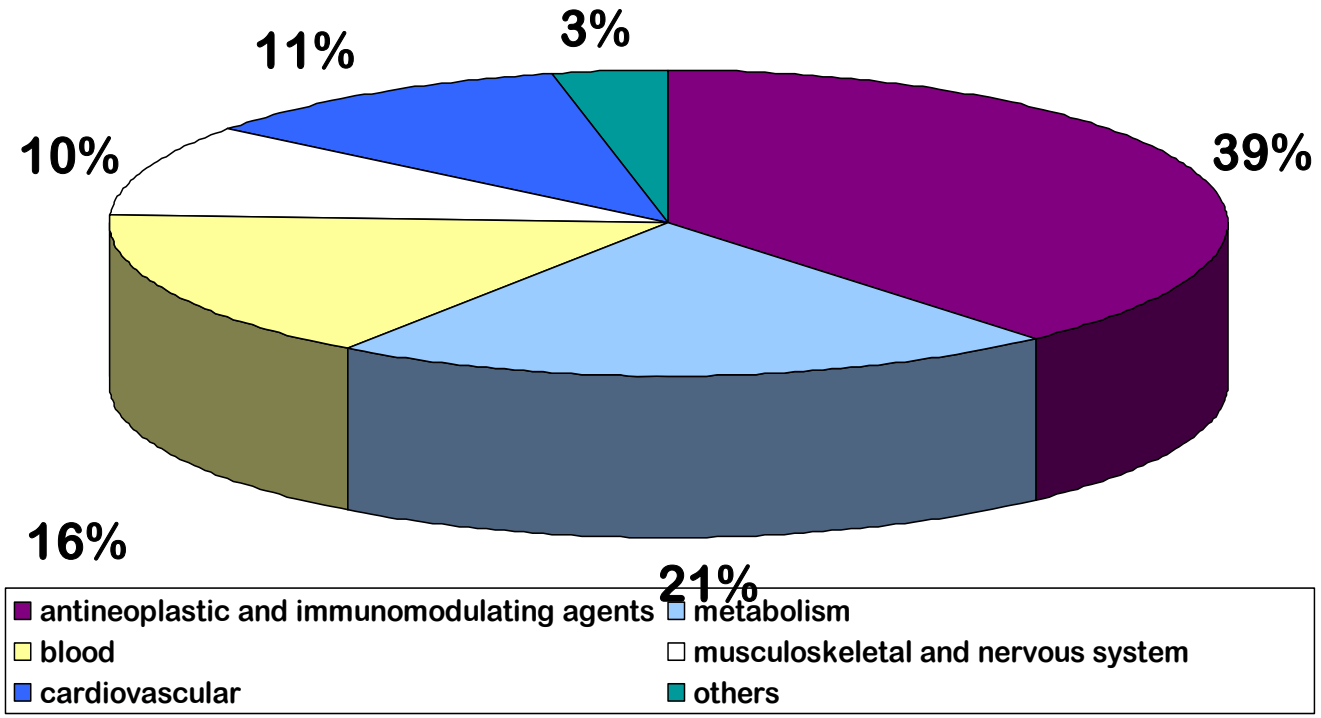
OD by therapeutic field



MA in ten years

- 63 orphan designated products authorised
- More than half (51%) for orphan diseases affecting less than 1 in 10,000 patients
- Average time OD to MA is 3 years
- Authorisations
  - 38% under exceptional circumstances
  - 6% conditional approval

Orphan products authorised per therapeutic area



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What information is public today?

Orphan designation

COMP monthly report (after opinion)

EU Commission Register of orphan designated medicinal products (after decision)

Public summary of positive/negative opinion for orphan designation (after decision)

Position on the removal of a designated orphan medicinal product from the community register (COMP monthly report)

Position on review of criteria for orphan designation at time of MA (from 2010)

Public summaries of opinion

Publication of public summaries of opinions

- summary main aspects designation
- accessible language
- Contact point sponsor
- Contacts patient organisations

Information for “competitors”

Proactive publication of products that start marketing authorisation procedure (COMP and CHMP monthly reports)

Information about review orphan status at time of authorisation

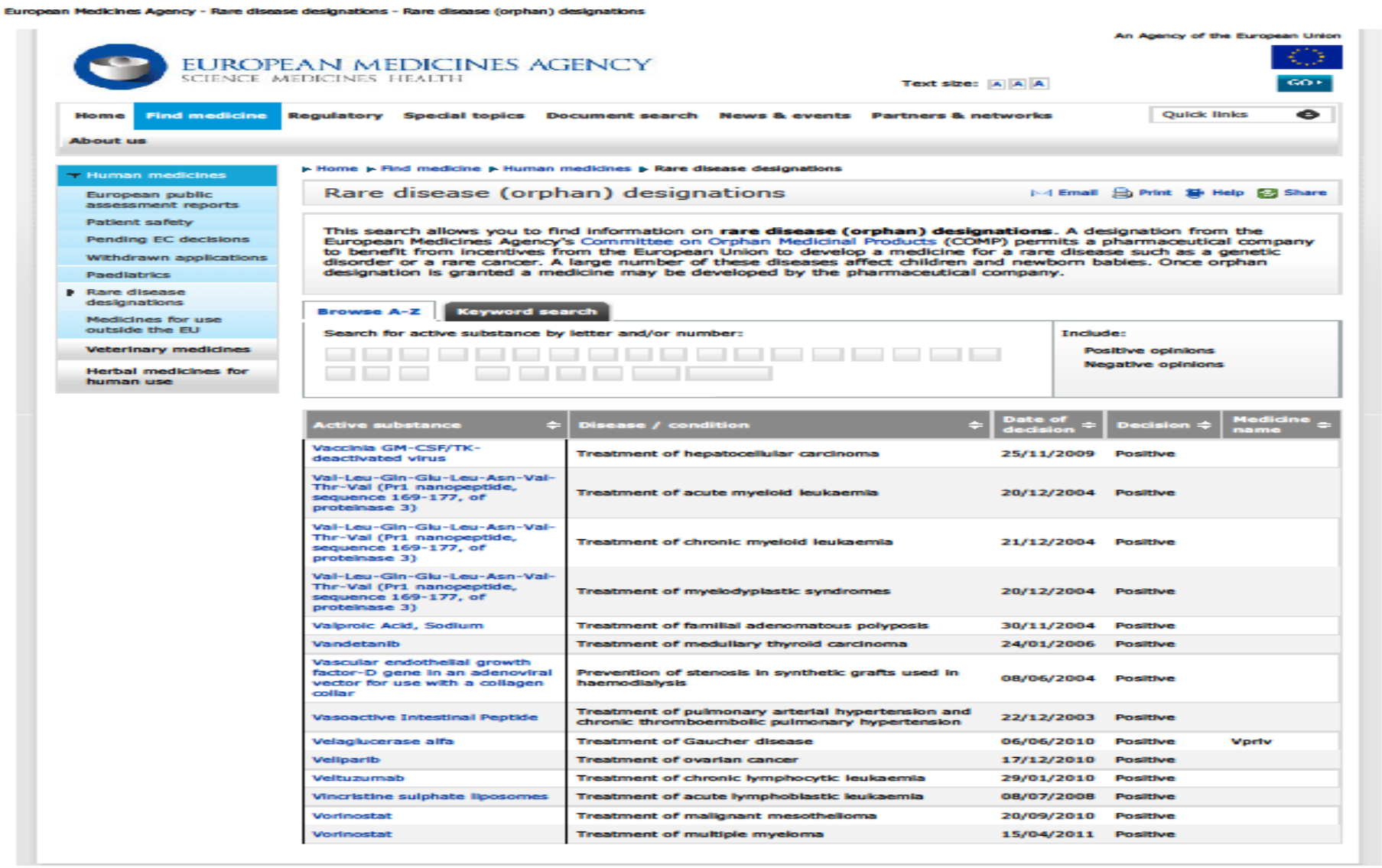
Summary of COMP position on the review on web

Includes information on

- prevalence
- seriousness
- and significant benefit if applicable

Link to EPAR and viceversa

Publication for 2010 completed



European Medicines Agency - Rare disease designations - Rare disease (orphan) designations

An Agency of the European Union

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Rare disease (orphan) designations

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This search allows you to find information on **rare disease (orphan) designations**. A designation from the European Medicines Agency's Committee on Orphan Medicinal Products (COMP) permits a pharmaceutical company to benefit from incentives from the European Union to develop a medicine for a rare disease such as a genetic disorder or a rare cancer. A large number of these diseases affect children and newborn babies. Once orphan designation is granted a medicine may be developed by the pharmaceutical company.

Browse A-Z | Keyword search

Search for active substance by letter and/or number:

Include:
Positive opinions
Negative opinions

Active substance	Disease / condition	Date of decision	Decision	Medicine name
Vaccinia GM-CSF/TK-deactivated virus	Treatment of hepatocellular carcinoma	25/11/2009	Positive	
Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3)	Treatment of acute myeloid leukaemia	20/12/2004	Positive	
Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3)	Treatment of chronic myeloid leukaemia	21/12/2004	Positive	
Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3)	Treatment of myelodyplastic syndromes	20/12/2004	Positive	
Valproic Acid, Sodium	Treatment of familial adenomatous polyposis	30/11/2004	Positive	
Vandetanib	Treatment of medullary thyroid carcinoma	24/01/2006	Positive	
Vascular endothelial growth factor-D gene in an adenoviral vector for use with a collagen collar	Prevention of stenosis in synthetic grafts used in haemodialysis	08/06/2004	Positive	
Vasoactive Intestinal Peptide	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension	22/12/2003	Positive	
Velaglucerase alfa	Treatment of Gaucher disease	06/06/2010	Positive	Vpriv
Veliparib	Treatment of ovarian cancer	17/12/2010	Positive	
Veltuzumab	Treatment of chronic lymphocytic leukaemia	29/01/2010	Positive	
Vincristine sulphate liposomes	Treatment of acute lymphoblastic leukaemia	08/07/2008	Positive	
Vorinostat	Treatment of malignant mesothelioma	20/09/2010	Positive	
Vorinostat	Treatment of multiple myeloma	15/04/2011	Positive	

http://www.ema.europa.eu/...kwByEnter=false&alreadyLoaded=true&status=Positive&status=Negative&startLetter=V&keyword=Enter+keywords&searchType=Active+Substance[17/05/2011 13:29:11]

EU/3/10/752

Orphan designation | Key facts | Review of designation

On 6 June 2010, orphan designation (EU/3/10/752) was granted by the European Commission to Shire Pharmaceuticals Ireland Limited, Ireland, for velaglucerase alfa for the treatment of Gaucher disease.

Expand all items in this list

- What is Gaucher disease?
- What is the estimated number of patients affected by the condition?
- What treatments are available?
- How is this medicine expected to work?
- What is the stage of development of this medicine?
- Opinions on orphan medicinal product designations are based on the following three criteria:

Name	Language	First published	Last updated
EU/3/10/752: Public summary of positive opinion for Velaglucerase alfa for the treatment of Gaucher disease	(English only)	23/06/2010	18/10/2010

Related information

Vpriv: EPAR

Sponsor's contact details:

Shire Pharmaceuticals Ireland Limited
5 Riverside Walk
Citywest Business Campus
Dublin 24
Ireland
Telephone: +353 1 4297700
Telefax: +353 1 4297701

 7 Westferry Circus . Canary Wharf . London E14 4HB . Tel +44 (0)20 7418 8400 . Fax +44 (0)20 7418 8416

Many thanks

any questions?

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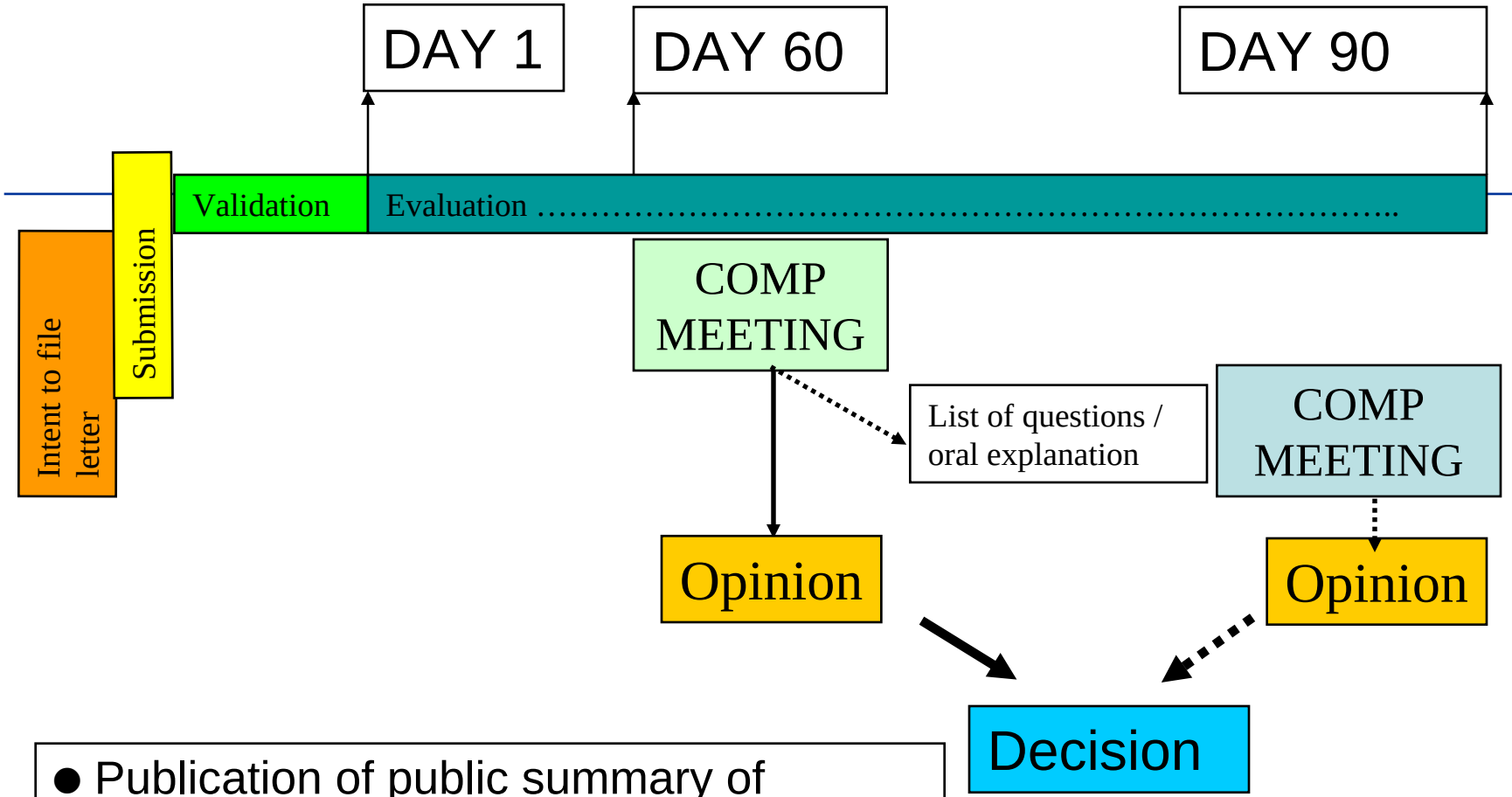
EMA website: http://www.ema.europa.eu

Back up slides



- Publication of public summary of opinion

(lay language) on EMEA website

Authorisation of an orphan drug

Based on same standards as for non orphan products (quality / safety / efficacy)

Authorisation only centralised procedure

CHMP responsible for assessment

Authorisation within designated condition

More than one designation possible per product (independent incentives)

Specific requirements MAA (I)

Assessment of similarity (WHEN ORPHAN IS ON MARKET)

- Applies if other orphan medicines authorised for same designated condition
- Need to submit report in module 1.7
  - Molecular structure
  - Mechanism of action
  - Similarity of indication (“significant overlap of populations”?)
- Assessment by CHMP working party competent
- Final opinion by CHMP
- Similarity can be triggered any time before EC decision
- Proactive publication ongoing procedures

Specific requirements MAA (II)

Maintenance designation criteria

- Report to orphan medicines section
  - At time of submission MA
  - Possible to update
- Need to address all designation criteria
- Standard set at time of authorisation
- Assessment by COMP; opinion after MA opinion by CHMP

Procedure

Sponsor submits report at the same time submission marketing authorisation application

Procedure allows two discussions at COMP

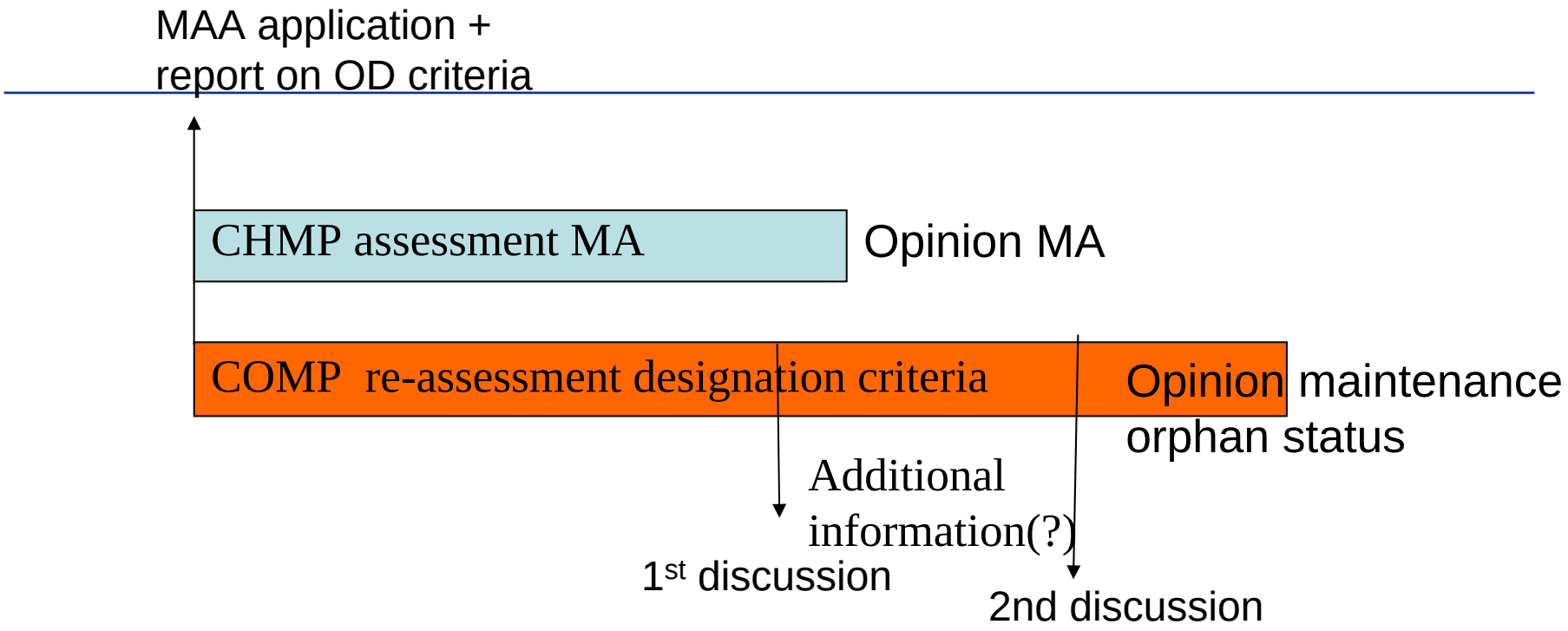
COMP adopts opinion only after CHMP has adopted opinion on marketing authorisation

Possibility to invite sponsor for oral explanation

COMP opinion can be subject to appeal

Final COMP opinion is sent to Commission

·····Opinion


MAA application +
report on OD criteria
CHMP assessment MA
Opinion MA
COMP re-assessment designation criteria
Opinion maintenance orphan status
Additional information(?)
1st discussion
2nd discussion

COMP and CHMP roles