EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Fostering orphan medicines development

IRDiRC conference, Dublin 2013

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An agency of the European Union

Can regulators foster development?

Principal role is regulating medicines

- Can regulators be indifferent to failures or lack of development?

Need to stay away from being directly involved

- Data /results assessment, central to regulators, should be done independently
- Need to ensure there are no conflicts of interest

Fostering orphan drug development

Medicines development

Economic incentives

Support to research

Do we have a "regulatory" tool?

Fostering orphan drug development

Medicines development

- Orphan designation and protocol assistance

Economic incentives

- Fee reductions and market exclusivity

Support to research

- COMP advisory role to EC on policy for orphan medicines

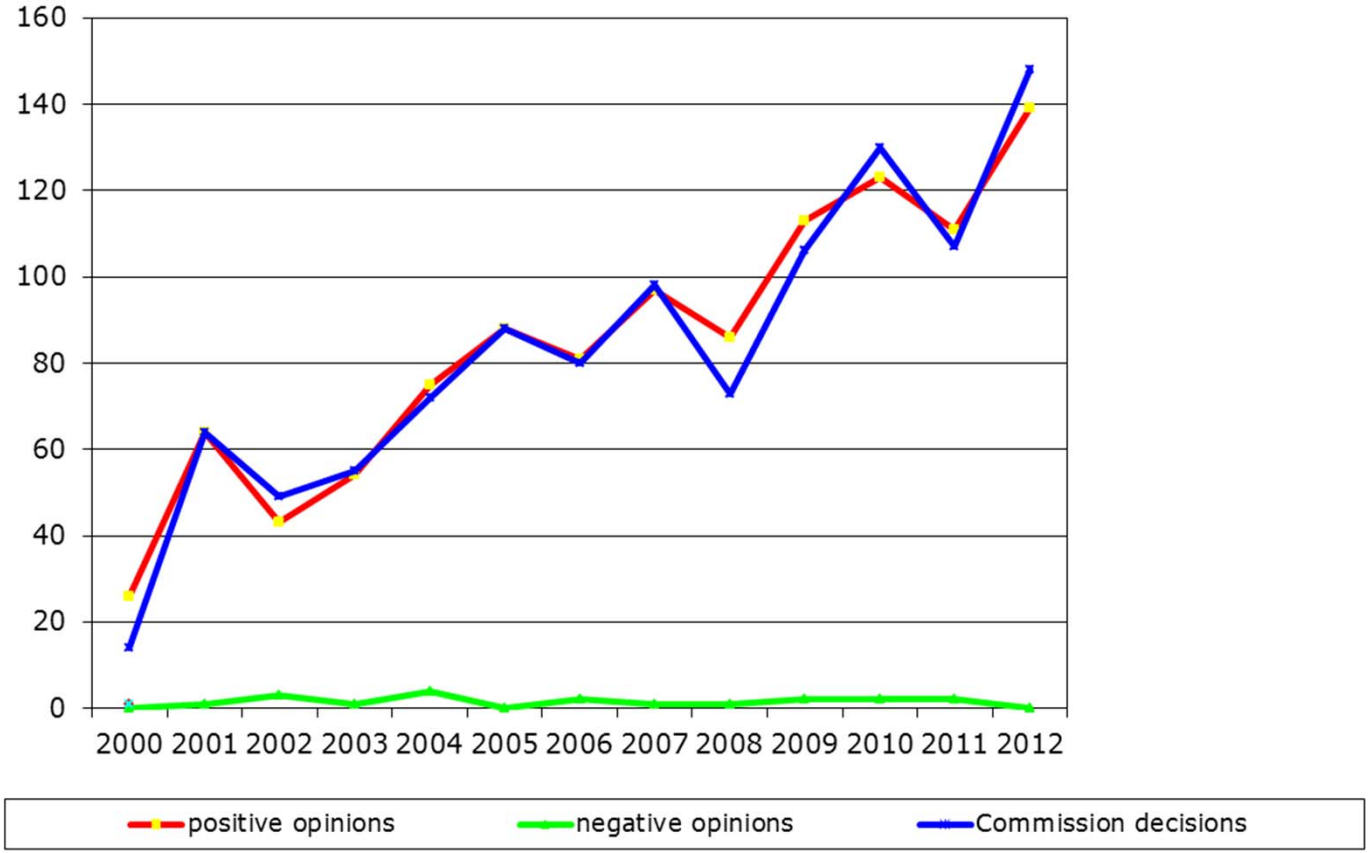
Regulation (EC) No 141/2000

Principles on orphan designation

Objective of Regulation (EC) No 141/2000

- provide incentives that stimulate research and development
- modify market conditions
- set up system of recognition for orphan medicines to be eligible for incentives:
  - Rarity (not more than 5 in 10,000)
  - Seriousness (life threatening / chronically debilitating)
  - Existence of alternative methods of treatment (significant benefit?)

Evolution orphan medicines designations



Protocol assistance

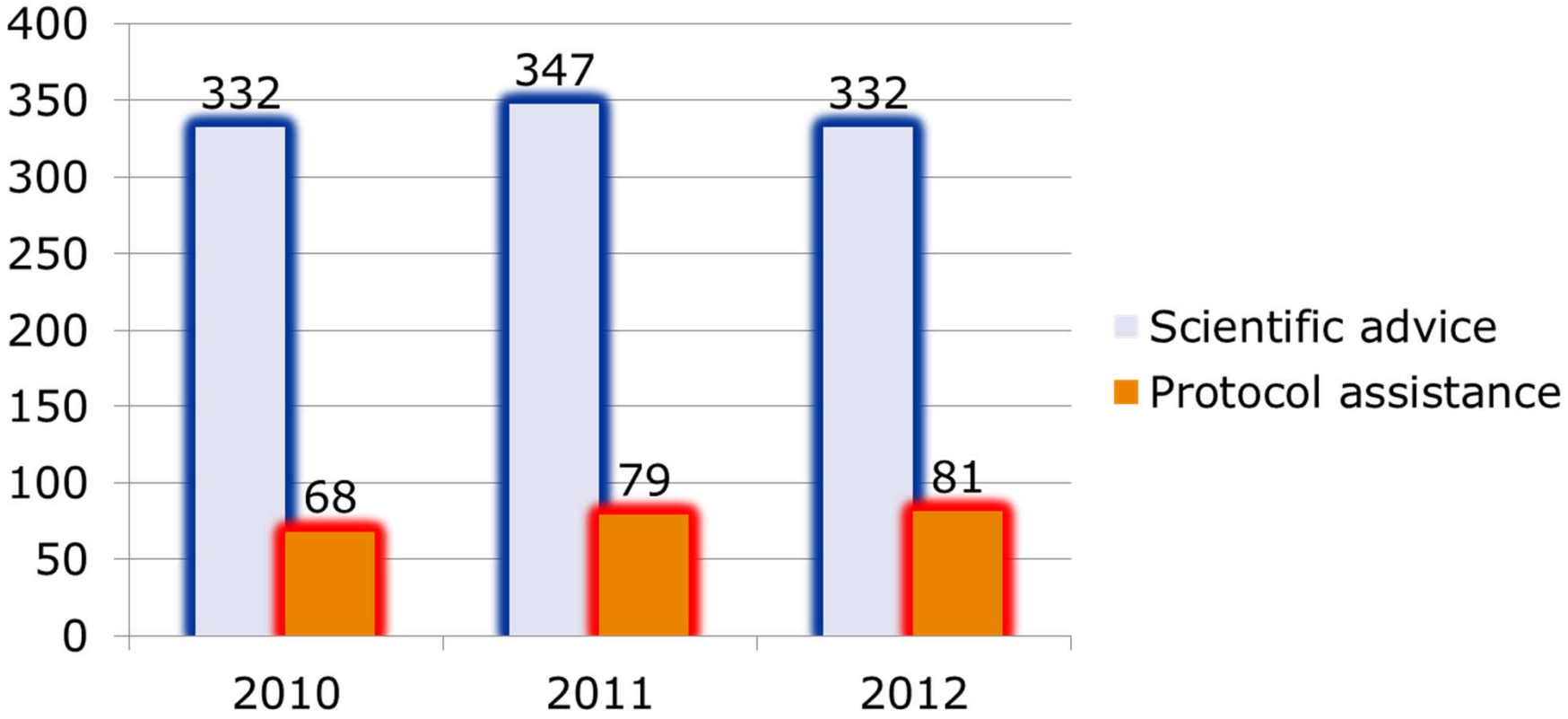
Provides Agency (EU Wide) advice on drug development

- clinical (90%; 51% exclusively) *
  - *(most relevant key development step)
- preclinical (44%)
- quality (27%)**
  - ** (most relevant development step for advanced therapies)

Possibility of biomarker qualification

Following advice increases chances of marketing authorisation (RR 1.48; failure rate non compliant 70%; compliant 2%)

Protocol assistance



Fee reductions

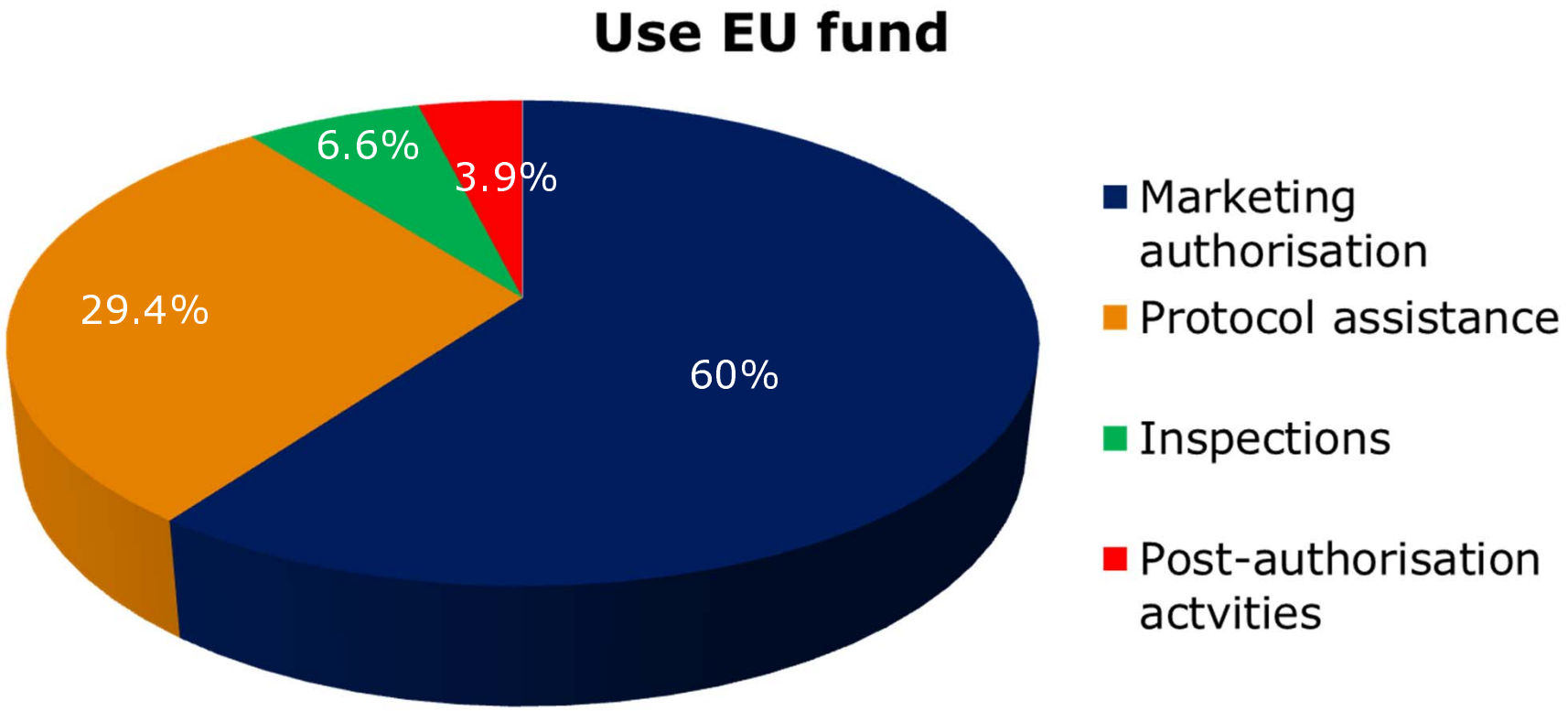
Annually EU allocated special fund to cover fee reductions (approx. 6 million Euro)

EMA has consistently kept maximum coverage for SMEs

Academia and SME responsible for 79% development of advanced therapies

Policy reviewed annually, needed revision in 2013 according to current budget

Allocation funds for fee reductions (2012)



Status of Orphan Marketing Authorisation Applications: 78 granted to date

Adopted positive opinion

- 1 awaiting decision

Ongoing applications in review process

- 27 applications in review process

Variations / Line Extensions in review process

- 3 applications in review process

Negative outcomes for orphan MAA

- 56 applications withdrawn
- 10 negative decisions/refusals

COMP advisory role

Regular exchange of information with EC to identify high level research needs

Access to information on development

Regulators have direct contact experience with successes and failures

Direct access to a wealth of information

International collaboration between regulators (USA, Japan, Canada)

Of the 12 projects in the article nine for orphan designated products

Cordis website: three additional projects granted that involve development of orphan drugs:

- Drugsford (inherited photoreceptor degeneration)
- Eurofancolen (fanconi anaemia)
- Aipgene (intermittent acute porfiria)

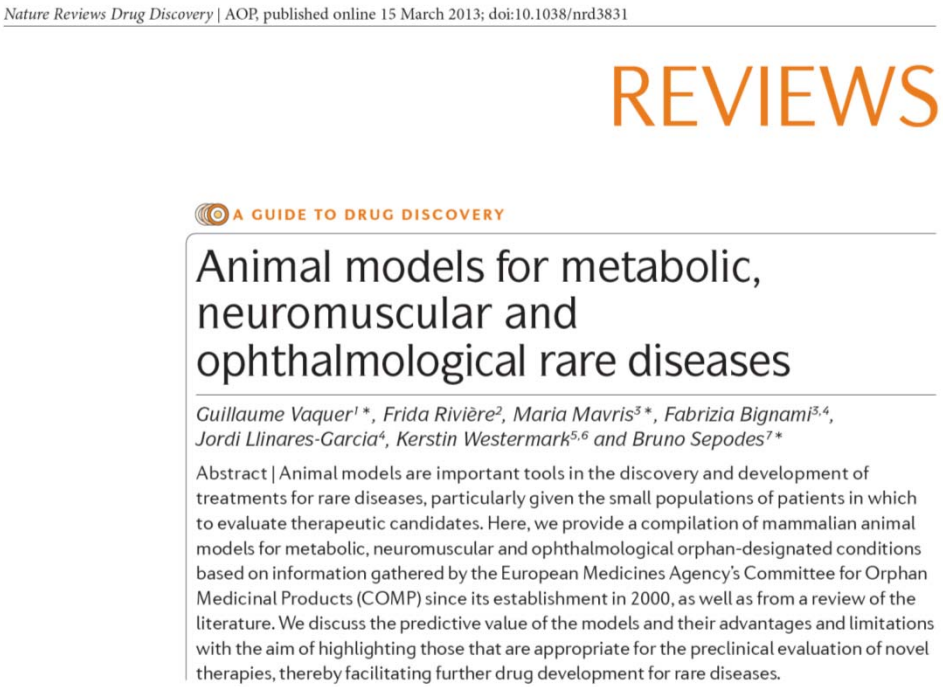
NATURE REVIEWS | **DRUG DISCOVERY** VOLUME 12 | APRIL 2013 | **253**

Rare disease project	Funding (million)
Neuromics: integrated European omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases	€12
RD-CONNECT: an integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research	€12
EURenOmics: European Consortium for high-throughput research in rare kidney diseases	€12
BALANCE: development of a bioartificial liver therapy in acute liver failure	€6
DevelopAKUre: clinical development of nitisinone for alkaptonuria	€6
FIGHT-HLH: first targeted therapy to fight hemophagocytic lymphohistiocytosis	€6
GAPVAC: glioma actively personalized vaccine consortium	€6
MeuSIX: clinical trial of gene therapy for mucopolysaccharidosis type VI — a severe lysosomal storage disorder	€6
Net4CGD: gene therapy for X-linked chronic granulomatous disease	€6
PREVENTROP: new approach to treatment of the blinding disease retinopathy of prematurity	€6
PROFNAIT: development of a prophylactic treatment for the prevention of fetal/neonatal alloimmune thrombocytopaenia	€6
Traumakine: interferon-beta treatment of acute respiratory distress syndrome	€6

Privileged access to knowledge

Suboptimal use:

- Lack of resources
- Confidentiality issues



Nature Reviews Drug Discovery | AOP, published online 15 March 2013; doi:10.1038/nrd3831

REVIEWS

A GUIDE TO DRUG DISCOVERY

Animal models for metabolic, neuromuscular and ophthalmological rare diseases

Guillaume Vaquer[1], Frida Rivière[2], Maria Mavris[3]*, Fabrizia Bignami[3,4], Jordi Llinares-Garcia[4], Kerstin Westermark[5,6] and Bruno Sepodes[7]**

Abstract | Animal models are important tools in the discovery and development of treatments for rare diseases, particularly given the small populations of patients in which to evaluate therapeutic candidates. Here, we provide a compilation of mammalian animal models for metabolic, neuromuscular and ophthalmological orphan-designated conditions based on information gathered by the European Medicines Agency's Committee for Orphan Medicinal Products (COMP) since its establishment in 2000, as well as from a review of the literature. We discuss the predictive value of the models and their advantages and limitations with the aim of highlighting those that are appropriate for the preclinical evaluation of novel therapies, thereby facilitating further drug development for rare diseases.

Fostering orphan drug development

Medicines development

- Orphan designation and protocol assistance
- Scientific validation / guided development

Economic incentives

- Fee reductions and market exclusivity
- Economic viability

Support to research

- COMP advisory role to EC on policy for orphan medicines
- Knowledge "repository" and target identification – public regulatory intelligence