ORPHANDEV, ACCELERATOR PLATFORM FOR THE DEVELOPMENT OF ORPHAN DRUGS

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INTRODUCTION

The European Union (EU) introduced a new legislation in 2000 in order to stimulate the research and development of orphan drugs. This regulation establishes a centralised procedure for the designation of orphan medicinal products and puts in place incentives for the research, development and marketing of orphan medicinal products (Regulation (EC) No 141/2000) [1]. 15 years after, this disposal is a success, with 1406 designated orphan medicinal products (January 1st 2015). However, this regulation remains poorly known by the academic sector while it is often at the origin of the proof-of-concept and the creation of start-ups.

15 YEARS OF ORPHAN DESIGNATION IN EUROPE

The procedure:

Pre-submission meeting with EMA *Optional but strongly recommended*
Submission of the application *According to the EMA deadlines*
Validation by EMA *(day 1)*
Evaluation by the COMP *(Committee for Orphan Medicinal Products)* → positive or negative opinion *(60 to 90 days)*
Evaluation by the European commission (EC) → final decision *(30 days)*

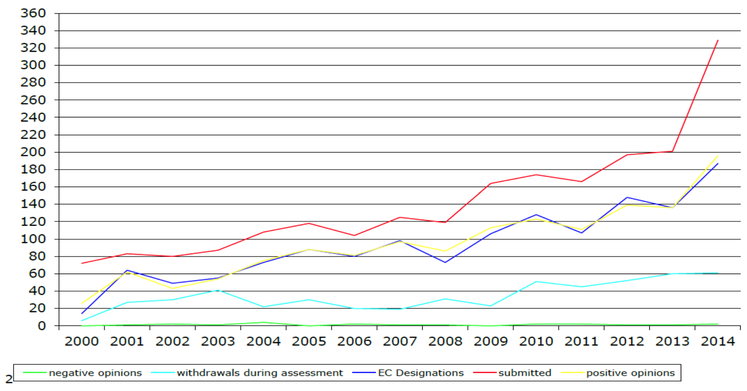

Fig1: Evolution during 15 years of the number of Orphan Applications [2]

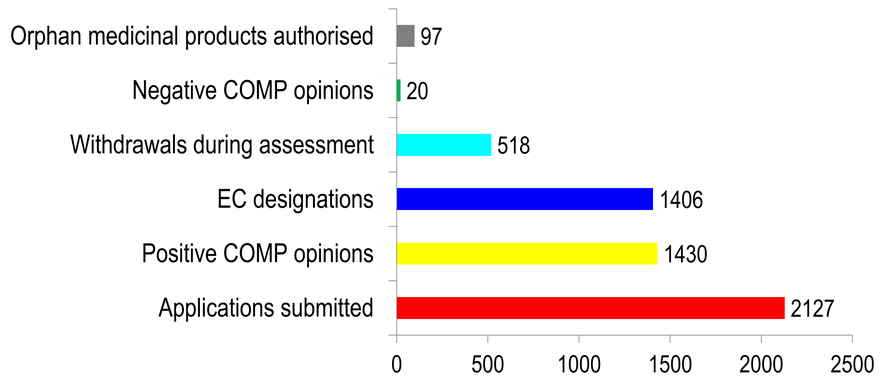

Fig 2: Total number of Orphan Applications in January, 1st 2015 [2]

The incentives:

- ✓ Fee reductions in the regulatory procedures at the EMA (ex: Protocol assistance, Marketing Authorisation Application (MAA))
- ✓ A 10 years commercial exclusivity after MAA in Europe and 7 years in the US
- ✓ Visibility and recognition of the project and its sponsor
- ✓ Eligibility for European calls for projects

Eligibility criteria:

- ✓ prevalence (< 1/2000, to be proven)
- ✓ medical plausibility (proof-of-concept)
- ✓ significant benefit (vs standard care)
- ✓ Life-threatening or debilitating condition

25% of the applications failed (negative COMP opinion or withdrawal during assessment)

➔ need to evaluate the admissibility of the application before submitting

Protocol assistance:

Aims to support sponsors to provide adequate data for benefit–risk assessment at the time of MAA
Compliance with recommendations on clinical trial design is correlated with [3]:

- ✓ Reduction in major objections
- ✓ Higher MAA success rate
- ✓ Shorter MAA procedure

ORPHANDEV: A SUPPORT FOR ORPHAN DESIGNATIONS

Mean time of the procedure	Months
Preparation of the application (until validation by EMA)	6,7
Evaluation by EMA (COMP) and EC	3

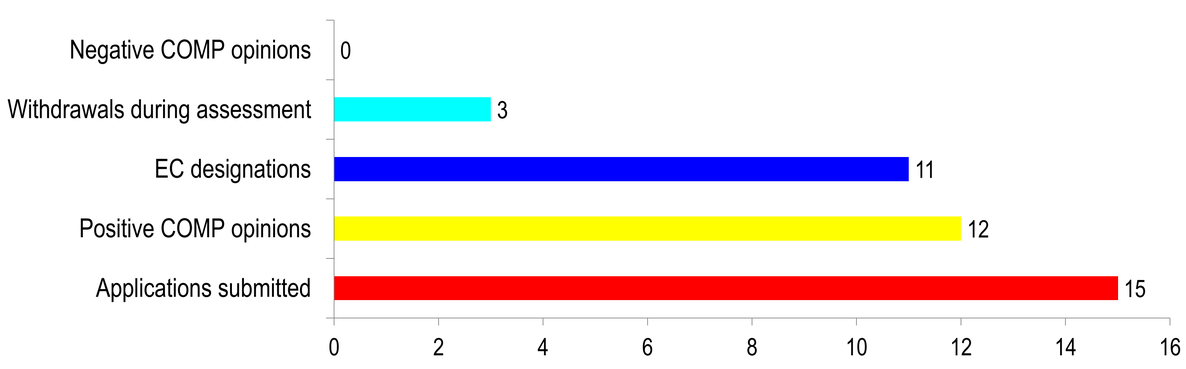

Fig 3: Number of orphan applications submitted with OrphanDev support (2013-2015)

REASONS FOR WITHDRAWAL OR NON-SUBMISSION	Prevalence
	Medical plausibility
	other
STAGE AT THE STOP OF PROCEDURE	Feasibility study
	Pre-submission meeting
	Withdrawal during assessment

OrphanDev information tools:

A pedagogical sheet:

OrphanDoc « The orphan designation »

A clinical research professionals' training:

Eudipharm's « Orphan Drug & Rare Disease Seminar »
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Orphan Drug & Rare disease Seminar

OrphanDev support reduces the risk of failure:

- ✓ 4 applications not submitted after the feasibility study
- ✓ only 3 applications were withdrawal during assessment

OrphanDev offers:

- ✓ Support for establishing a work calendar
- ✓ Support for drafting the scientific document
- ✓ Support for compiling the administrative dossier
- ✓ A specific expertise for a feasibility study before the submission assistance in the meetings with the agencies
- ✓ Submission and follow-up of the application

REFERENCES
[1] REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 1999 on orphan medicinal products
[2] EMA, Orphan Medicines Figures 2000/2014, Orphan Medicines - Product Development Scientific Support (update 01/01/2015)
[3] Hofer MP, Jakobsson C, Zafiropoulos N, Vamvakas S, Vetter T, Regnstrom J, Hemmings RJ. Regulatory watch: Impact of scientific advice from the European Medicines Agency. Nat Rev Drug Discov. 2015 May;14(5):302-3.