FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

PAVIA, ITALY
25 > 27 OCTOBER
2018

XI FORESIGHT TRAINING COURSE

CHANGES IN REGULATORY SCIENCES IN THE EU
how to move from a reactive
to a multi-stakeholder proactive attitude

ISTITUTI CLINICI SCIENTIFICI MAUGERI
Via Salvatore Maugeri, 6

Regulation (EC) 141/2000

Fondazione per la Ricerca Farmacologica Gianni Benzi onlus

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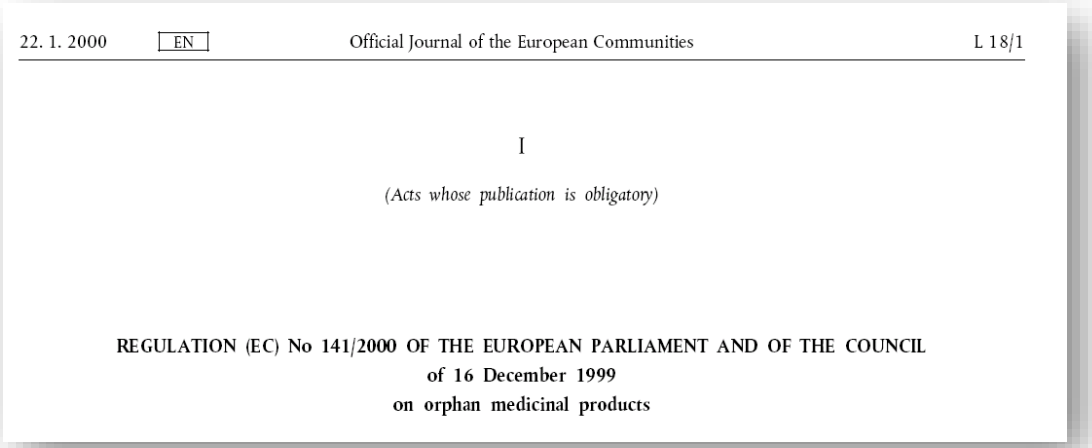

22. 1. 2000 EN Official Journal of the European Communities L 18/1

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(Acts whose publication is obligatory)

REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 16 December 1999
on orphan medicinal products

- **Criteria for designation** (Art. 3)
- **Committee for Orphan Medicinal Products** (Art. 4)
- **Procedure for designation and removal from the register** (Art. 5)
- **Protocol assistance** (Art. 6)
- **Community marketing authorization** (Art. 7)
- **Market exclusivity** (Art. 8)
- **Other incentives** (*Art.* 9)

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Criteria for designation

1° CRITERIA

2° CRITERIA

Prevalence < 5 / 10 000

alternatively

Scarce investment return

Lack of alternative treatment

alternatively

Significant benefit to patients

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Procedure for designation and removal from the register

- Application for designation submitted at any stage of the development before MA application ⇨ EMA to verify the validity and prepare a summary report ⇨ opinion to be given within 90 days ⇨ EC decision within 30 days
- If negative opinion ⇨ the sponsor may submit detailed grounds for appeal
- Designated product entered in the ***Community Register of Orphan Medicinal Products***
- Sponsor to submit to EMA an annual report on the state of development of the product
- Possible transfer of the designation to another sponsor
- A designated orphan medicine to be removed from the Community Register:
  - at the request of the sponsor
  - if it is established before the market authorisation is granted that the designation criteria are no longer met
  - at the end of the period of market exclusivity

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Do we need to change something in procedures for designation?

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Committee for Orphan Medicinal Products

Works for

- Designation of orphan drugs
- Definition of the condition
- Medical plausibility of proposed product / disease
- Prevalence
- Assumption of significant benefit

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Do we need to improve something in COMP procedures and tasks?

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Incentives

Incentives	In EU
Marketing exclusivity	10 years + 2 if paediatric
Clinical development costs	–
Orphan designation	free of charge
Support from agency during the development process	free of charge protocol assistance
MAA	40% fee reduction; free of charge for SMEs and for paediatric products
Fee reductions for SMEs	90% of fee reduction for post authorisation inspections; free of charge pre-authorisation inspections, post-authorisation activities, including annual fees, during the first year after marketing authorisation
Public funds	(possible) incentives from EC (i.e. research grants)
	(possible) incentives in single Member States for research, development and MA

Giannuzzi V et al. Orphanet Journal of Rare Diseases. 2017 Apr 3;12(1):64

No mandatory incentives for research/clinical research!

Do we need more?

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Do we need more support from EMA and other institutions?

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European Commission

Ref. Ares(2017)6059807 - 11/12/2017

EVALUATION ROADMAP	
Roadmaps aim to inform citizens and stakeholders about the Commission's work to allow them to provide feedback and to participate effectively in future consultation activities. Citizens and stakeholders are in particular invited to provide views on the Commission's understanding of the problem and possible solutions and to share any relevant information that they may have.	
TITLE OF THE EVALUATION	Evaluation of the legislation on medicines for children and rare diseases (medicines for special populations)
LEAD DG – RESPONSIBLE UNIT	SANTE – B.5
INDICATIVE PLANNING (PLANNED START DATE AND COMPLETION DATE)	- Publication Roadmap (Q4 2017); - Start evaluation (Q1 2018); - End evaluation (Q3 2019).

- Rare diseases (it is estimated that 5000 to 8000 distinct rare diseases exist in the EU) identified as an area in which satisfactory treatment was not sufficiently available
- have patients' needs been fulfilled? what have been the societal consequences? what has been the synergy between the two?
- Focus on the cost-effectiveness when providing the incentives and rewards and how they have been used in practice, both from a general point of view and per group (patients, industry, payers etc)

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Benzi Foundation comments

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- Economic support for the clinical development costs not set out by the regulation
- Completing the R&D process still remains a challenging issue for an orphans
- The national lists of rare diseases should be updated, shared and harmonised across countries
- Notwithstanding efforts and cooperation between US and EU, regulatory procedures to gain the designation, terms and classifications to be harmonised
- In many EU Countries, patients have to wait a long period of time before the medicines, approved by the EC on the basis of the CHMP positive opinion, are really available ⇨ to push the activation of negotiation-price-reimbursement procedure right after the EU MA
- To refer to ERNs and their efforts