Medicines & Healthcare products Regulatory Agency

HCPWP meeting: COMP feedback September 2018

Dr Daniel O'Connor (UK COMP representative)
On behalf of the COMP

CPRD NIBSC MHRA

Importance of a valid orphan condition

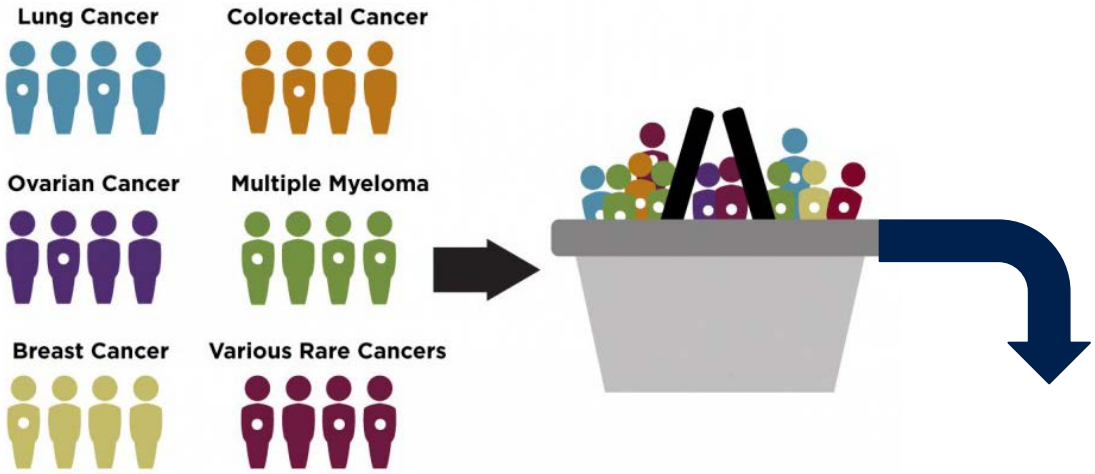
- Orphan designation starts with the condition – without it COMP cannot evaluate any of the other criteria

  - A condition is understood as any deviation 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)

  - The condition is a critical first component – **needs to be rare**!

- COMP asks details on the aetiology, specific characteristics, histopathology, clinical characteristics, classification, diagnosis and symptoms

Novel Trial Designs



- Increasingly drug development programmes are supported by novel clinical trial designs
- E.g. basket study which relies on extrapolation of evidence = challenges for orphan criteria

Therapeutic indication: treatment of unresectable or metastatic solid tumours with X mutation in patients who require systemic therapy

Traditional rare orphan conditions which may also express molecular marker	Rare molecular defined subset of common tumours	Common molecular defined subset of common tumours
Orphan designation	**? May meet the orphan designation criteria**	**Unlikely to meet orphan designation**

Image source: https://www.mskcc.org/blog/clinical-trial-shows-promise-basket-studies-drugs

Flexibility in the FDA approach to orphan drug development

Nina L. Hunter, Gayatri R. Rao and Rachel E. Sherman

Scientific advances, in combination with government incentives and commercial opportunity, have fuelled strong investment in orphan drugs, resulting in many innovative therapies.

- **FDA:** will need to take advances in genomics and precision medicine into account as it considers what constitutes an orphan 'disease or condition'
  - Whether a disease should be defined in a tissue specific or tissue agnostic manner?
  - Current scientific understanding may support the designation and approval of certain drugs across multiple rare tumour types
  - As more targeted therapies are developed, more drugs may qualify for orphan designation based on orphan subsets
  - how a disease is defined and whether a valid orphan subset exists may need to be refined

- **EU:** 'subsetting' a condition with the use of biomarkers will not be acceptable unless the sponsor provides solid scientific evidence that the activity of the product would not be shown on the larger population

COMP paper on defining the orphan condition

- Discusses challenging areas when delineating an orphan condition

- Four main sections:
  - Symptoms of a disease
  - Subsetting - severity/ stages and biomarkers
  - Iatrogenic and adverse reactions to a medicinal product
  - Treatment modalities

- Provides an at-a-glance chart of available guidance

COMMENT

Defining orphan conditions in the context of the European orphan regulation: challenges and evolution

Daniel J. O'Connor[1,12], Maria E. Sheean[2,3,12], Matthias P. Hofer[2,12], Stelios Tsigkos[2], Segundo Mariz[2], Laura Fregonese[2], Kristina Larsson[2], Virginie Hivert[4], Kerstin Westermark[5], Frauke Naumann-Winter[6], Violeta Stoyanova-Beninska[7], Ingeborg Barišić[8], Giuseppe Capovilla[9], Armando Magrelli[10] and Bruno Sepodes[11]*

The definition and acceptability of an orphan condition is pivotal for the assessment of European orphan medicinal product designation applications, and consequently the eligibility for incentives. Here, based on the experiences of the Committee for Orphan Medicinal Products, we discuss how to define orphan conditions in the context of the European regulatory framework.

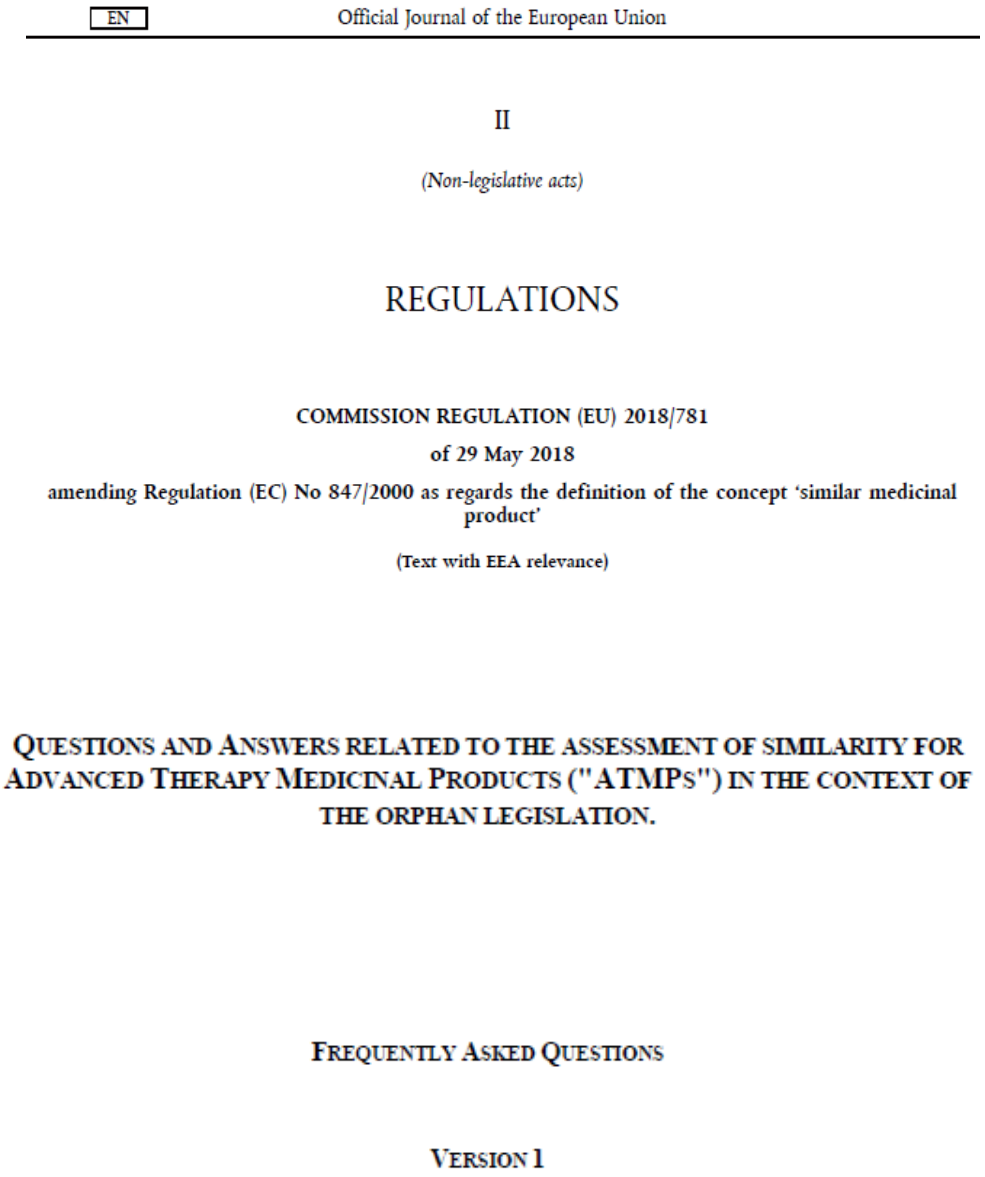
- Explains COMP decisions in the context of the EU orphan drug regulation and provides some discussion points to help future sponsors

EC activities

- Regulation (EC) No 847/2000 provides a definition of 'similar medicinal products' for the purposes of the application of the incentives provided under the Regulation

- Due to major developments in the field of biological medicines and technical progress including advanced therapy medicinal products (ATMPs), the definitions required adaption

- Two new documents released by the EC in May 2018 to reflect changing science



EN Official Journal of the European Union

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) 2018/781

of 29 May 2018

amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'

(Text with EEA relevance)

QUESTIONS AND ANSWERS RELATED TO THE ASSESSMENT OF SIMILARITY FOR ADVANCED THERAPY MEDICINAL PRODUCTS ("ATMPS") IN THE CONTEXT OF THE ORPHAN LEGISLATION.

FREQUENTLY ASKED QUESTIONS

VERSION 1

EMA activities

- An overview of the EU's orphan designation programme provided in a infographic →

- Questions and answers document addresses some common misunderstandings ↓

28 February 2018
EMA/551338/2017

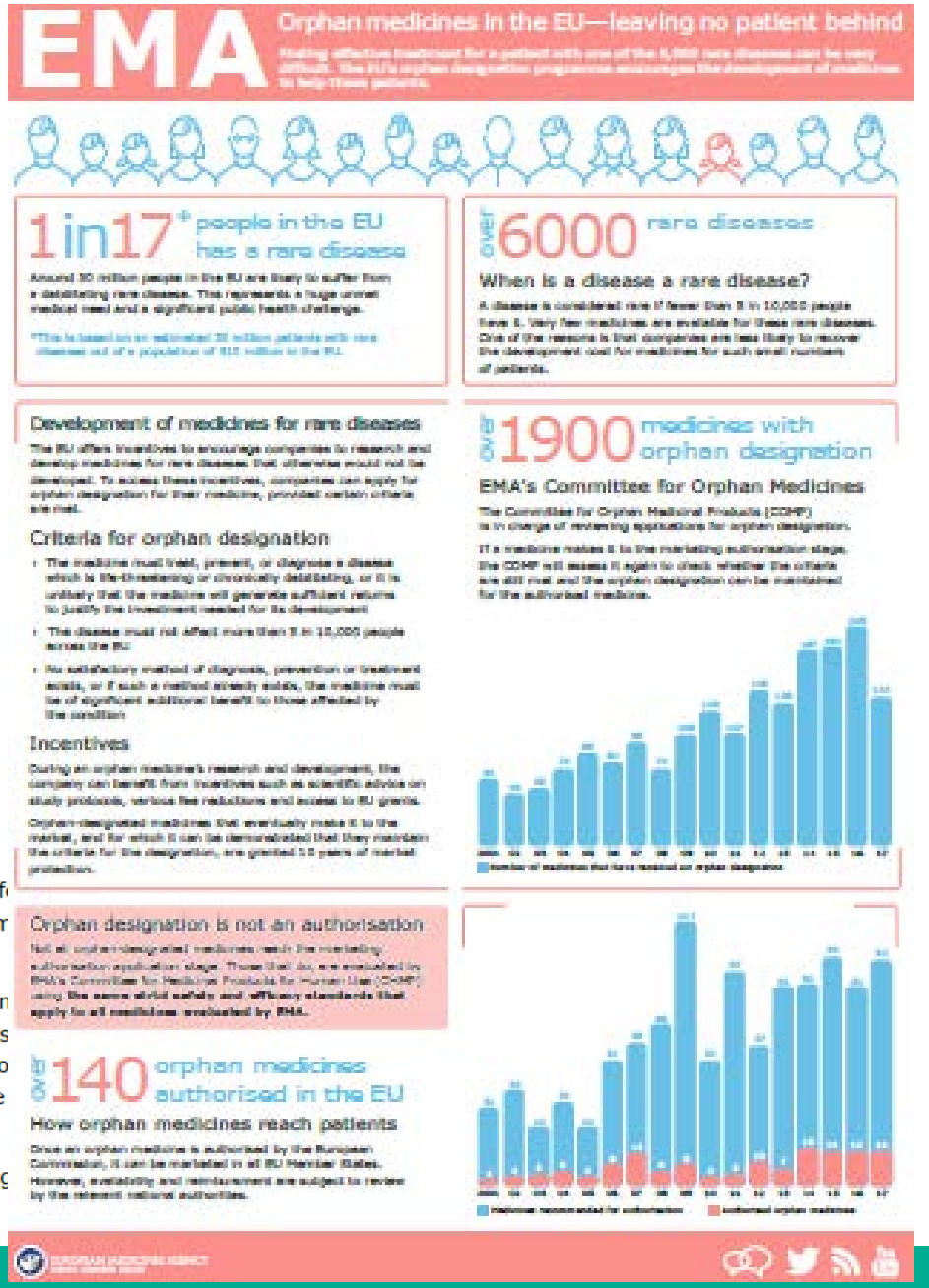
Rare diseases, orphan medicines

Getting the facts straight

EMA is eager for European citizens with rare diseases to have access to specific and eff
medicines. The European Union's orphan legislation has been designed to help overcom
hurdles these medicines face to get on the market.

Broadly speaking, the orphan legislation foresees giving orphan designation for substan
be used for treating, preventing or diagnosing a rare and serious condition. Orphan des
help the medicine's developer advance the medicine to the stage where it can be autho
on the market. Formal approval (marketing authorisation) is needed before a medicine
marketed.

Misunderstandings often arise about orphan medicines and how orphan designation is g
following questions and answers address some common ones.



Thank you

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