EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clinically Relevant Advantage and Major Contribution to Patient Care

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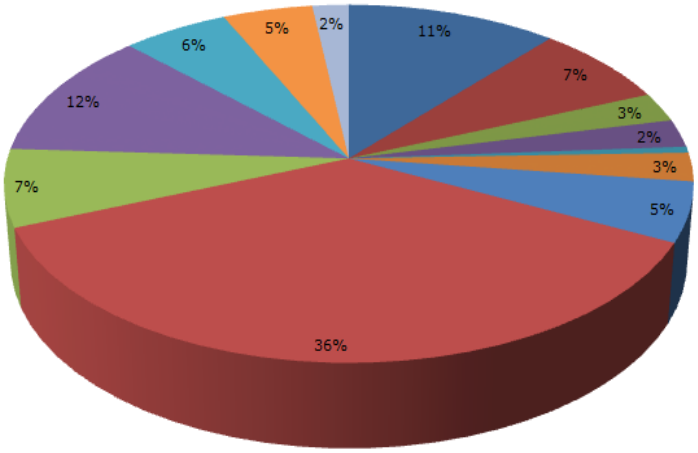
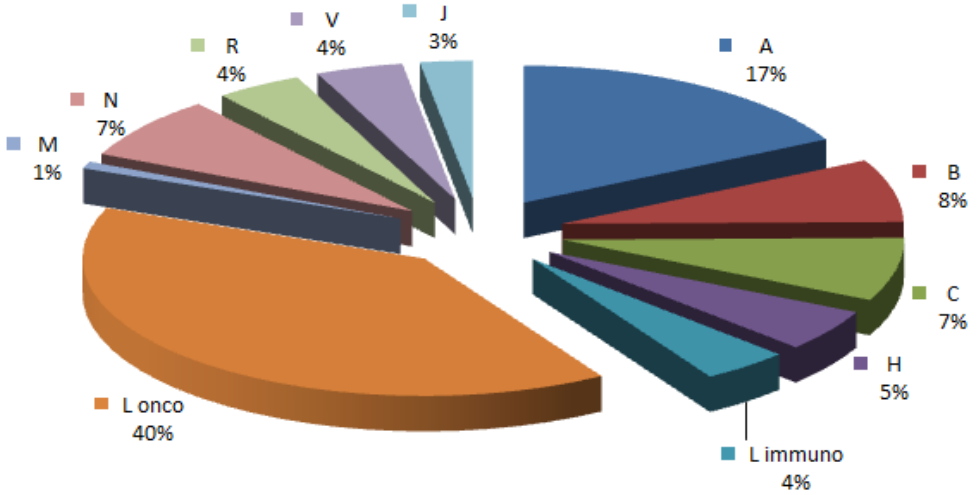
Conflict of interest: none

Orphan Medicinal Products (2000-2014)



Orphan designations (OD)
n=1430



Orphan Medicinal Products at MA
n=105

A Alimentary tract and metabolism; **B** Haematology; **C** Cardiovascular system; **H** Systemic hormonal; **J** Antiinfectives for systemic use ; **L** Immunology; **L** Antineoplastic; **M:** musculoskeletal**; N** Nervous system; **R** Respiratory system; **V** Various

Satisfactory methods ≠ Comparators

Satisfactory

- authorized medicinal products for the condition
- non pharmacological methods part of standard of care

Comparators for determination of SB?

OD

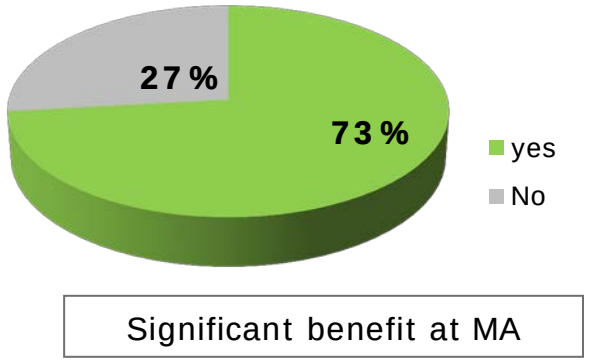
- overall condition (comparative discussion)
- preclinical data supporting claims whenever possible

MA

- therapeutic indication/position in standard of care
- different comparators for different grounds
- includes recently authorized products

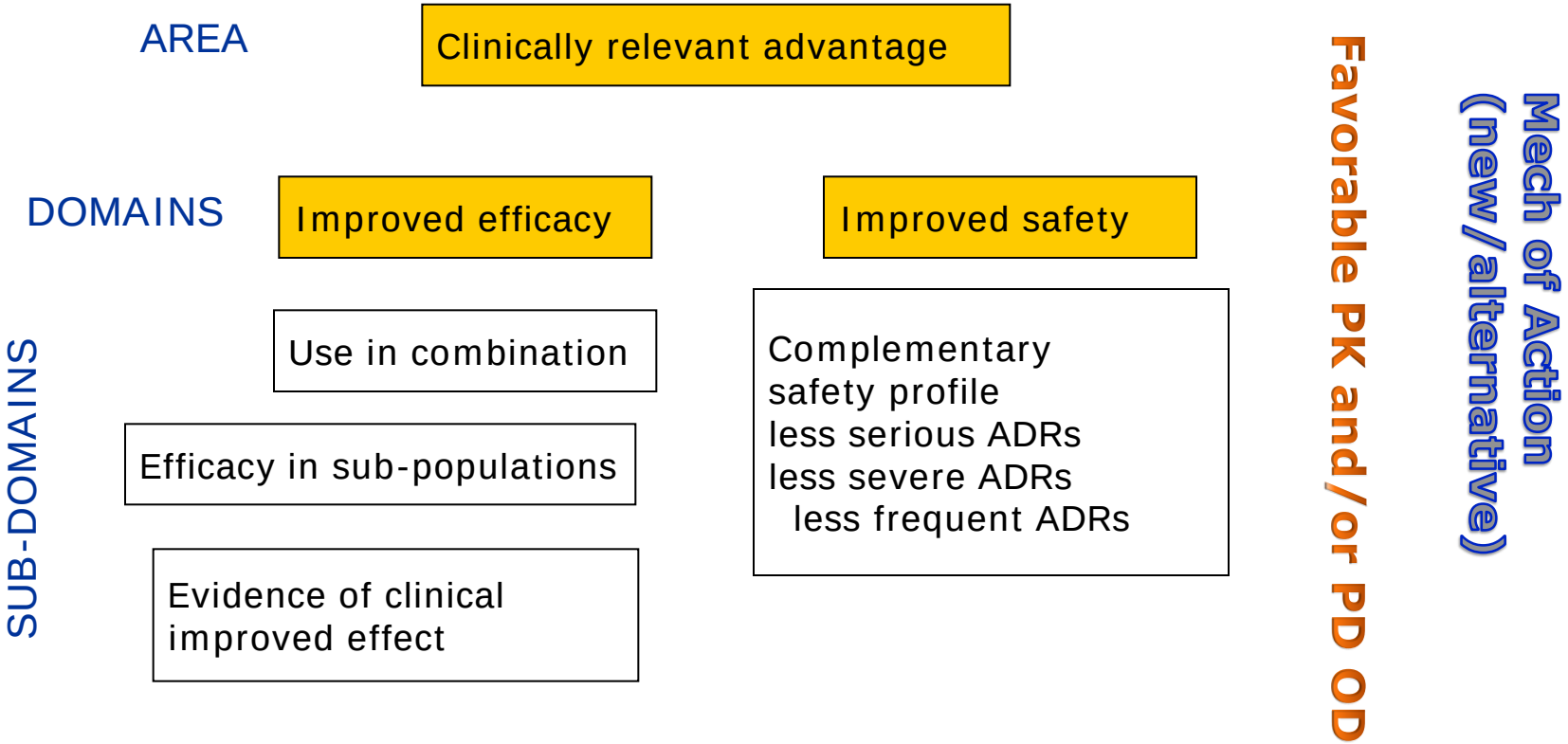
Significant benefit concepts

- Retrospective analysis of COMP reports at OD and MA of authorized OMPs 2000-2014
- Identification of scientific concepts and of domains and sub-domains within the two main areas of SB
- Criteria for definition of domains and-sub-domains:
  - EMA/COMP/15893/2009 Recommendations
  - working experience of the COMP
  - sound scientific and pharmacological concepts



Significant benefit at MA

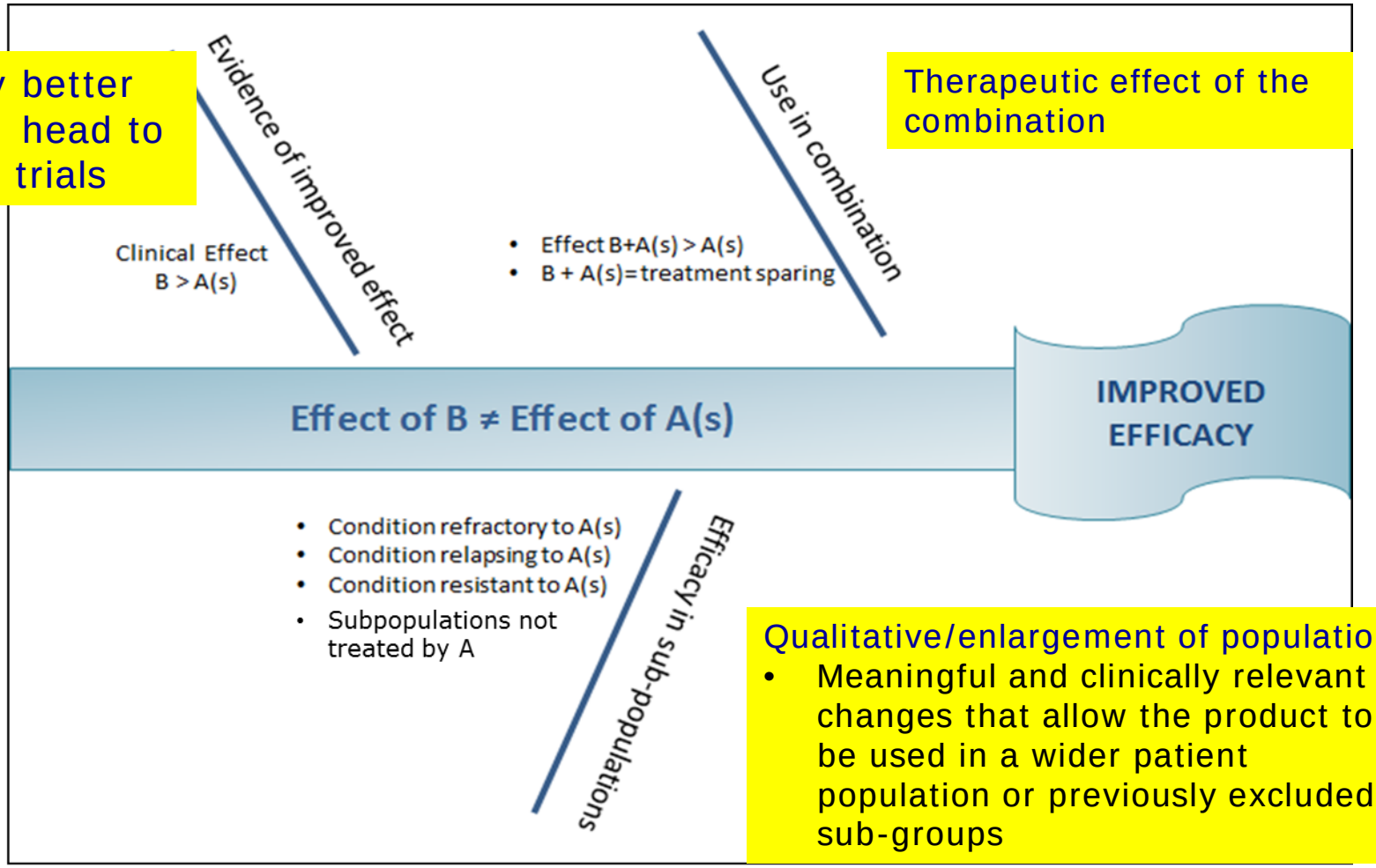
Conceptual grounds (I)



(grounds not mutually exclusive, i.e. one product can have more than one ground

Improved efficacy

Ideally better efficacy head to head trials



Therapeutic effect of the combination

Qualitative/enlargement of population

- Meaningful and clinically relevant changes that allow the product to be used in a wider patient population or previously excluded sub-groups

Conceptual grounds (II)

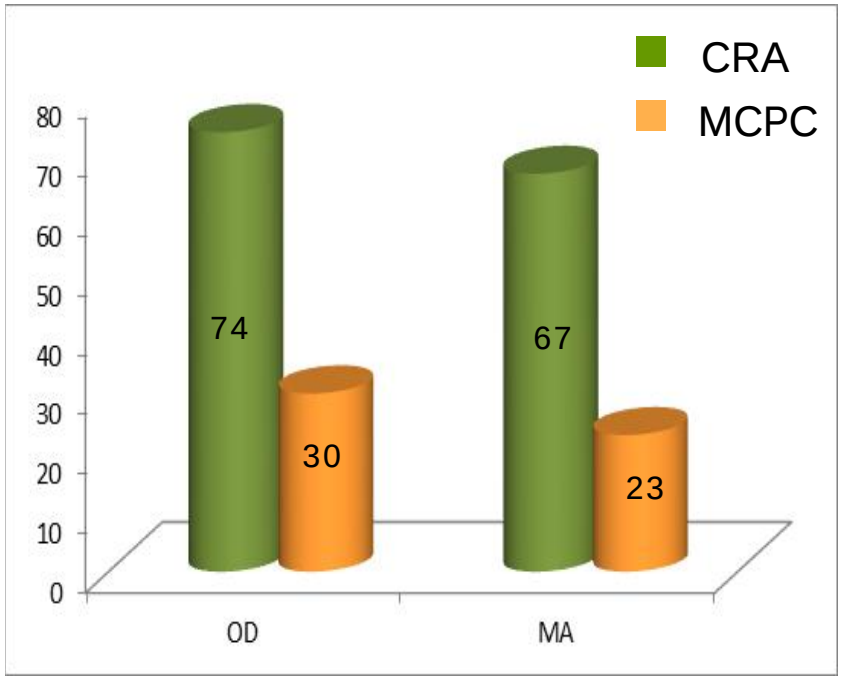
AREA: Major contribution to patient care

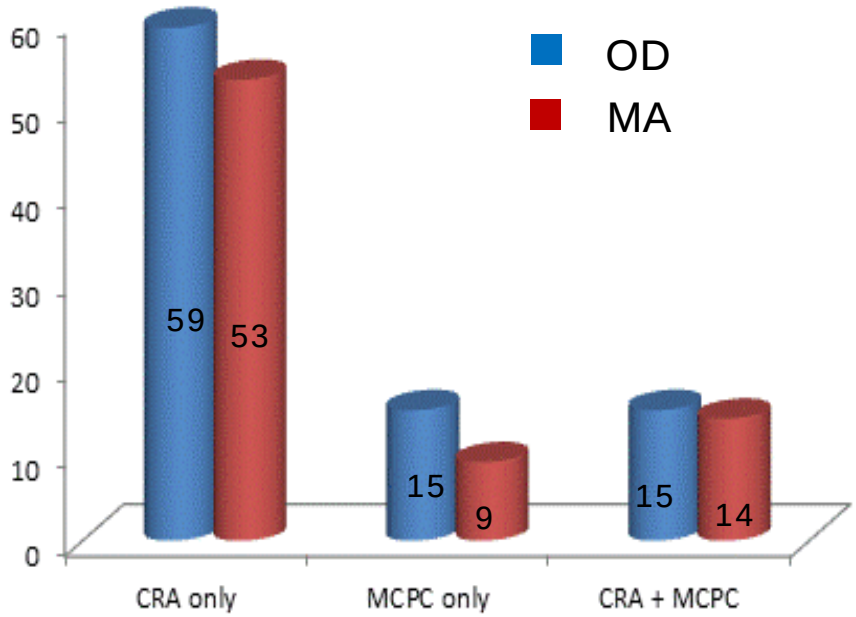
DOMAINS: Availability; Ease of use

SUB-DOMAINS: Shortage of supply/ Improved availability from EU authorization; Formulation/administration route; Dosing schedule; Other

Favorable PK and/or PD OD

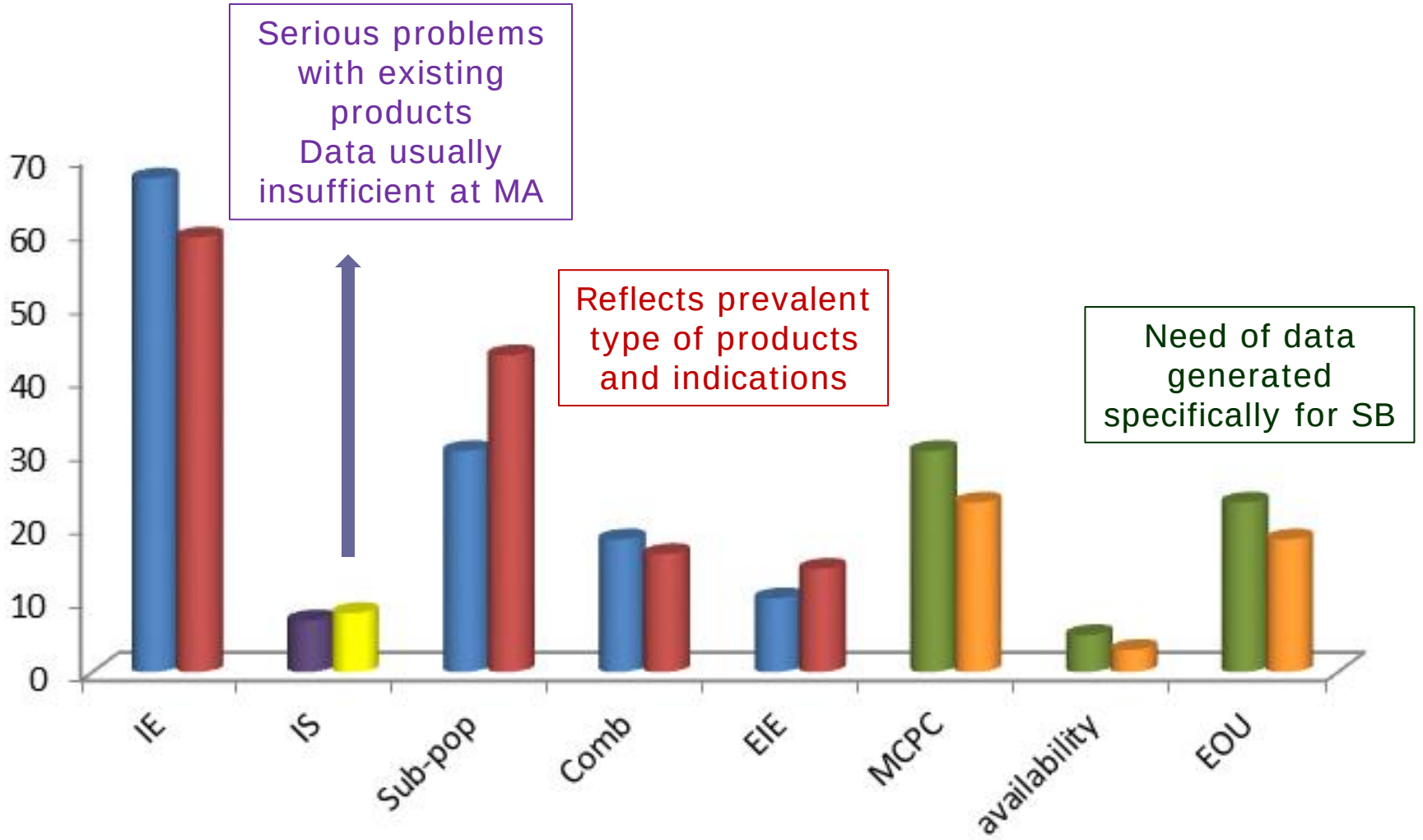
Clinically Relevant Advantage and Major Contribution to Patient Care





(Figures include products withdrawn before MA and after OE in the COMP, and products with more than 1 MA)

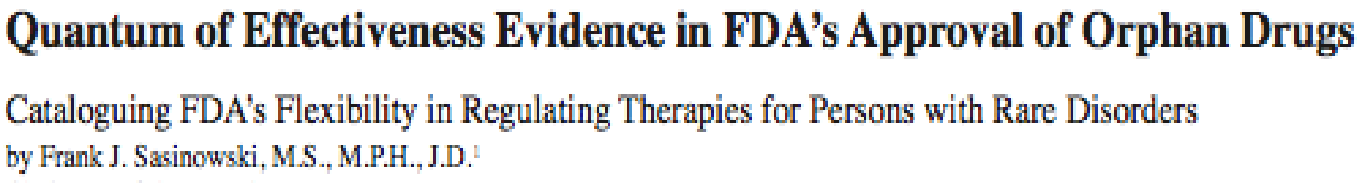
Distribution of grounds



(Figures include products withdrawn before MA and after OE in the COMP, and products with more than 1 MA)

Challenges of clinically relevant advantage

Data generation in rare diseases


Quantum of Effectiveness Evidence in FDA's Approval of Orphan Drugs

Cataloguing FDA's Flexibility in Regulating Therapies for Persons with Rare Disorders

by Frank J. Sasinowski, M.S., M.P.H., J.D.[1]

- Limited data sets, natural history, difficulties in studying subgroups
- Minimum clinical relevant advantage (e.g. last li

Breakout session 2

Crowded areas (SB *vs* several products at the same time)

- Role of indirect comparisons, data other than RC
  controls, registries. Same class, sequential treatments

Breakout session 1

- **Parallel development**

Challenges of major contribution to patient care

- Data for MCPC collected in pivotal trials for orphan MA often sub-optimal (non validated instruments, limited data-sets)
- Role of PROs? Core outcome measures vs. subjectivity
- Balance between generation of instruments for large number and heterogeneous rare diseases and case by case decisions on self-evident advantages as base of SB? (oral vs. IV, portability)
- How to quantify ease of administration, convenience, less monitoring needs, etc…? role and methodology of patient preferences

Breakout session 3

Thank you

Acknowledgements

- COMP, SB-Working Group,
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- Breakout session moderators

Questions?