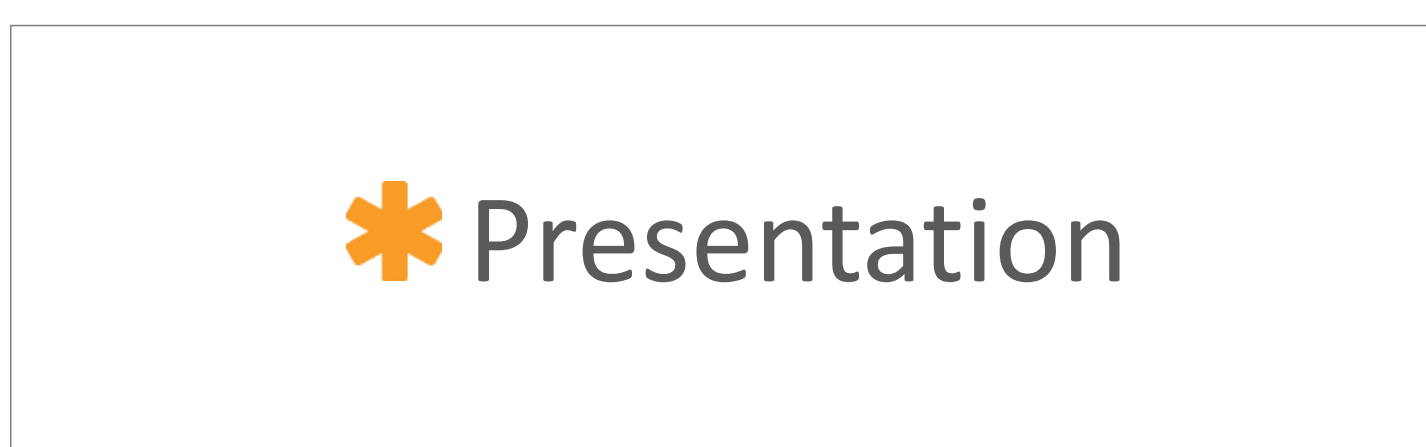
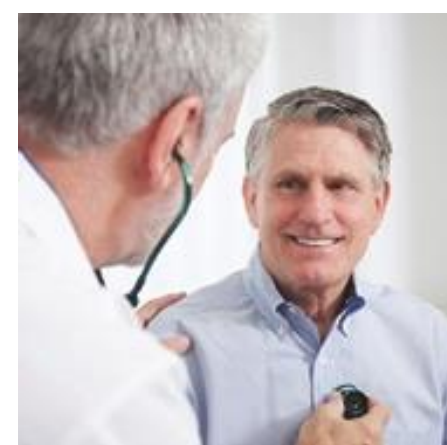




European Federation of Pharmaceutical
Industries and Associations

Proposals for coordination of HTA across Europe: implications for rare diseases

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Outline



- * **Challenges in the assessment of RDs therapies and review of recommendations**
to improve HTA practices for RDs
- * **The relative efficacy /effectiveness dilemma in OMPs**
- * **Evidence requirement EMA vs HTA**
- * **Potentialities of EUnetHTA JA3 for RDs**
- * **Sharing final reflections**

RD can be challenged by HTA practices....



- * If EBM standards are the only criteria for positive assessments
- * If CEA is a major principle for positive appraisal
- * If ethical considerations are far from being systematically addressed
- * If patients perspectives are not taking into account in in HTA



Because....

- * Randomized controlled study designs for clinical efficacy estimations are difficult to conduct due to low prevalence of diseases and group heterogeneity (high level of mutations).
- * Current used clinical effectiveness assumptions are not taking into account the heterogeneity of severity and distinct disease evolution.
- * QALY uses an utility instrument that has been not validated for RD (1-3)
- * Patients perspectives are not yet effectively taken into account in R&D and HTA

Some recommendations from scientific and policy literature to improve HTA for RDs

- * For the assessment, acceptability of a multi-method approach (the best possible quantitative and qualitative evidence)
- * For appraisal and decisions, transparent multi-criteria including an explicit moral approach (utilitarianism vs egalitarianism; subjective vs normative)
- * For economic evaluations:
 - Do measure also the comparative use of health care, social and family resources.
 - In budget impact analysis, do not use just cost per patient as comparator with other more prevalent therapies. Take in to account the epidemiology of diseases (low prevalence!!) then, project expenses over time to compare.

* Increase patient effective engagement in both R&D and HTAs

* In summary : A more holistic value framework is needed for RD



1. Karen Facey, Alicia Granados, Gordon Guyatt et al Generating HTA evidence for rare diseases. International Journal of Technology Assessment in Health Care, 2014 30:4 (2014), 416–422
2. Erik Nord et al. QALYs: Some Challenges. Value in Health 2009 , 12 S 1
3. Bradley C. Johnston et al. Limited responsiveness related to the minimal important difference of patient-reported outcomes in rare diseases. Journal of Clinical Epidemiology 79 (2016) 10e21
4. www.irdirc.org/wp-content/uploads/.../SPCT_DraftDocument.pdf
5. Health Technology Assessment and Orphan Medicines paper from EFPIA/EuropaBio Joint Task Force on Rare Diseases and Orphan Medicinal Products 2014

Relative efficacy vs relative effectiveness a dilemma, specially in RDs



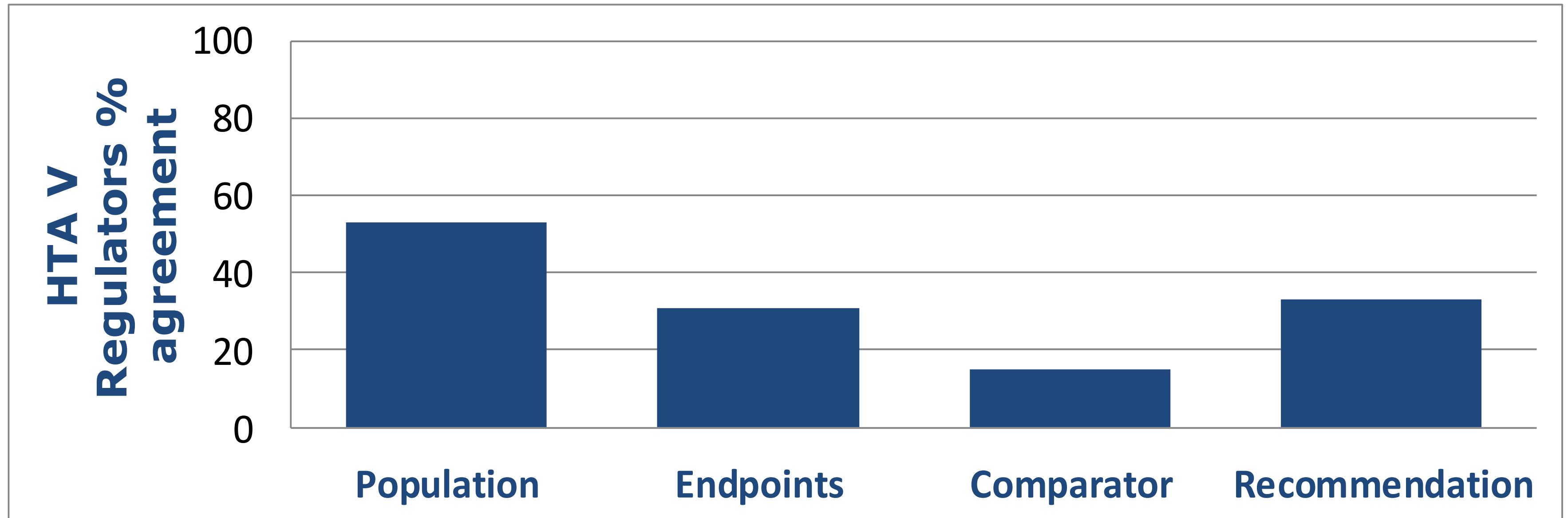
* High Level Pharmaceutical Forum 2008 (and all scientific literature)

* Relative efficacy is defined as the extent to which an intervention does more good than harm (effect of an intervention) , measured and compared with one or more treatment alternatives , under ideal (experimental) circumstances

* Relative effectiveness is the same, but measured under routine circumstances of health care and clinical practice

* **Currently at launch in RD, only efficacy information is available. Relative effectiveness can only be projected/predicted/modelled ... and in RDs, with heterogeneous populations, most of the results of relative effectiveness projections are far from what happens in the real world**

Level of agreement in product-specific evidence requirements EMA vs HTA
















N = 56 products

<http://www.efpia.eu/documents/189/61/HTA-Accelerator-In-Depth-Analysis-Final-report>

EUnetHTA Joint Action 3

An opportunity for OMPs



		DG SANTE and CHAFEA 					
		Work Package 1 Network Coordination - Dutch Health Care Institute 					
EUnetHTA Assembly	Executive Board	Work Package 2 Dissemination	Work Package 3 Evaluation	Work Package 4 Joint Production	Work Package 5 Evidence Generation	Work Package 6 Quality	Work Package 7 Implementation
		Lead: AETS-ISCIH 	Lead: TLV 	Lead: NIPHNO  Co-lead: LBI  ZIN 	Lead: HAS  Co-lead: GBA 	Lead: IQWiG  Co-lead: KCE 	Lead: NICE  Co-lead: Agenas 
		Spain	Sweden	Norway	Austria	Netherlands	Germany
		United Kingdom	Belgium	Croatia	Cyprus	Czech Republic	Denmark
		Finland	France	Greece	Hungary	Ireland	Latvia
		Malta	Poland	Portugal	Romania	Slovakia	Slovenia
Italy	Estonia	Lithuania	Bulgaria	Switzerland			

How does agenda for EU HTA cooperation fit with industry OMP priorities?

* Industry recommendations around evidence and uncertainty **could fit well with EU**

HTA collaboration, for example:

- * HTA bodies have the opportunity to recognise their important role in managing uncertainty in the evidence. For ex: defining standards for **outcomes driven MEA**
- * HTA and regulatory bodies have the **opportunity to align** in their requirements to help companies develop the best evidence at different time-points of the life cycle.
- * HTA bodies can discuss and agree on the criteria for **accepting the value of evidence beyond RCTs in RDs : RWE!!**

* Industry recommendations on multi-stakeholder involvement **fit very well with** early parallel EMA/HTAs advice and all related options

So.. what's the benefit of HTA collaboration for OMPs?



- * Like for any other products, get to know each other better !
- * Align evidence requirement regulators/HTAs, HTAs/HTAS early on, and continuously in product life cycle : joint scientific advice involving EMA (CHMP SAWP and COMP) and the EUnetHTA Standing Committee
- * Align on the core of additional evidence needed for both regulatory and HTAs after launch
- * Share expertise (especially clinical experts) and provide the disease-specific context for evidence expectations and interpretation.
- * Increase patient effective engagement in early dialogues
- * Discuss and agree on the level and criteria for the acceptability of the multi-method approach to generate best possible evidence in areas of small populations, limited knowledge and dispersed evidence.

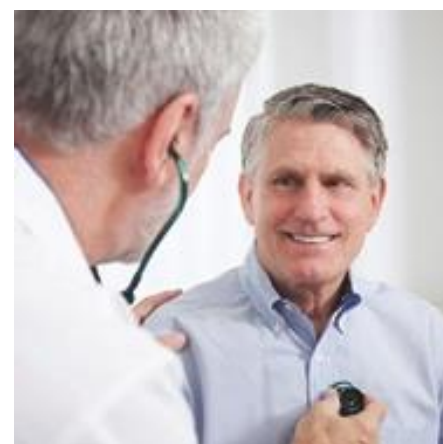
In summary:





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THANKS



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