



# EMA-HTA Parallel Scientific Advice



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**Why is this needed?  
Where do we want to get to?**

## **The Patient Advocate View**



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# EURORDIS' Objectives

**To achieve the quickest access to  
as many safe, efficient  
and affordable medicines  
with a real therapeutic added value,  
for all rare disease patients  
in the European Union**

# Toward a new sustainable business model for innovative rare disease therapies

- **Times are changing: Economic pressure & Demographic pressure on healthcare budgets / RD scientific opportunities from translational research & Stratified therapies / Growing investors expectations / Society sustainability & values**
- **The current business model of OMPs is not sustainable**
- **An evolution not a revolution**
- **The risks of not acting now**
- **Look at essential & long term common interest at stake across patients, across companies, across competent authorities, rather than antagonising the short term & short take diverging interest**
- **Corporate responsibility & leadership & policy innovation**

# KEY CONCEPTS

- **RD Treatments Evidence Generation is a Continuum**
- **Flexibility of Regulators should become an Official Policy**
- **Focus on Effectiveness beyond Quality, Safety and Efficacy**
- **Bridging the Gap Between EU Centralised Regulatory Decision and National Decisions on Pricing & Reimbursement**
- **Enhancing the Dialogue Between all Stakeholders all Along the Product Development & Life Cycle**

# Rare Disease Treatments Evidence Generation is a Continuum !

- **Marketing Authorisation is not anymore an on/off switch**
- **Better and broader collection of relevant data is needed**

**Data collected all along the life cycle of the medicine on risks as well as on benefits:**

- **Clinical trials**
- **Compassionate use**
- **Real life studies (actual heterogeneous population and real life constraints beyond clinical trials)**
- **Off label use**

# Flexibility of Regulators Should Become an Official Policy

- **Regulators are flexible (based on EMA and FDA experience) but need to say it clearly →**  
**in order for the process to be more visible, predictable, attractive and with more consistent scientific opinions**
- **Regulators need to have a supportive approach: Being a Gate Keeper is not good enough + Regulators should be Partners for Successful developments**
  - **Conditional Approval**
  - **Need for an intense roll-over process of Scientific Advice & Protocol Assistance before and after MA**
  - **Adaptive clinical trial design**
  - **Next: Patients Progressive Access / Adaptive Licencing**

# Focus on Effectiveness Beyond Quality, Safety and Efficacy

- **Dialogue between regulators (EMA), HTA (EUnetHTA), sponsors, medical experts, patient representatives to adapt Clinical Trial designs, as early as possible** (ex: methodology in small population, de-link efficacy trials and safety trials, historical control)
- **Anticipate more the therapeutic value demonstration during the Pre-MA Research Activities** (ex: registries, natural history, Good Clinical Practice Guideline on Diagnostic & Care) through Protocol Assistance (EMA)
- Early dialogue between regulators (EMA) and HTA (EUnetHTA) is also important to **anticipate and adapt Post MA Data Generation**



# Bridging the Gap Between EU Centralised Regulatory Decision and National Decisions on Pricing & Reimbursement

- One way or another, HTA and Payers need to be involved in all procedural aspects at the EMA to be well informed about the reality of medical needs, the potential and reality of the product, the uncertainties and the pathway to generate additional evidence for well targeted patients and good medical practices
- An approach on pricing based on **Value**, means a common understanding of what is Value and earlier marketing authorisation also means an understanding of this value as well as what the uncertainties are

# MAIN PROPOSALS

- **Early Dialogue / scoping / de-risking : EMA + HTA + Payers + P0 + Experts**
- **RD Data Collection & Registries & Natural History Studies**
- **Clinical Trials : EU Expert Opinion + adaptive design & statistical methodology + alternative to animal models + surrogate endpoints**
- **Progressive Patient Access / Adaptive Licensing**
- **Stronger FDA – EMA Collaboration : Common Guidelines**
- **CAVOMP: EMA & HTA dialogue**
- **MOCA: Payers dialogue / Value Framework / Price negotiations**
- **Pan-European Managed Entry Agreements**
- **Differential Pricing**
- **National Measures in RD National Plans/ Strategies**

# Early Dialogue / Scoping / De-Risking

- **EU Pharmaceutical Forum's Guiding Principles on OMPs recommends “early dialogue”**
- **Corporate Responsibility's Mechanism of Coordinated Access to OMPs recommend “early dialogue”**
  - **Early dialogue** is a dialogue, at a very early stage of development between 1 company and all relevant stakeholders - **EMA, HTA, Payers, Medical Experts, Patients** -on a specific product & disease (or with several companies on a specific disease) – EMA Pilots, HTA pilots
  - Early dialogue enables to discuss a) the potential to address an unmet medical need (**scoping**) and b) the optimal research, regulatory, and health policy approach (**de-risking**)

# Clinical Trials

**Legislation:** Ongoing advocacy to improve the EU Regulation on Clinical Trials: call for a **European Expert Opinion** (centralised at and facilitated by the EMA, rather than national or local Expert Opinion) for clinical trials in rare diseases

**Regulators:** Promotion of **Adaptive clinical trial design & statistical methods** (Current EMA Guideline, further research for science based policy by regulators)

**Research:** Promotion of research on **alternative to animal models** for new validated in vivo models + Promotion of research on **biomarkers** and surrogate endpoints

# Progressive / Adaptive Licensing

- **Progressive Patients Access / Adaptive Licensing**

- For diseases which are severe, with no alternative therapies or non-satisfactory therapies

- Within current regulatory framework:

- Conditional Approval
- Progressive enlargement of targeted population treated based on hospital prescription & inclusion criteria
- Collection of data within post-MA research activities (safety, efficacy, effectiveness) including new pharmacovigilance legislation, risk management plan...

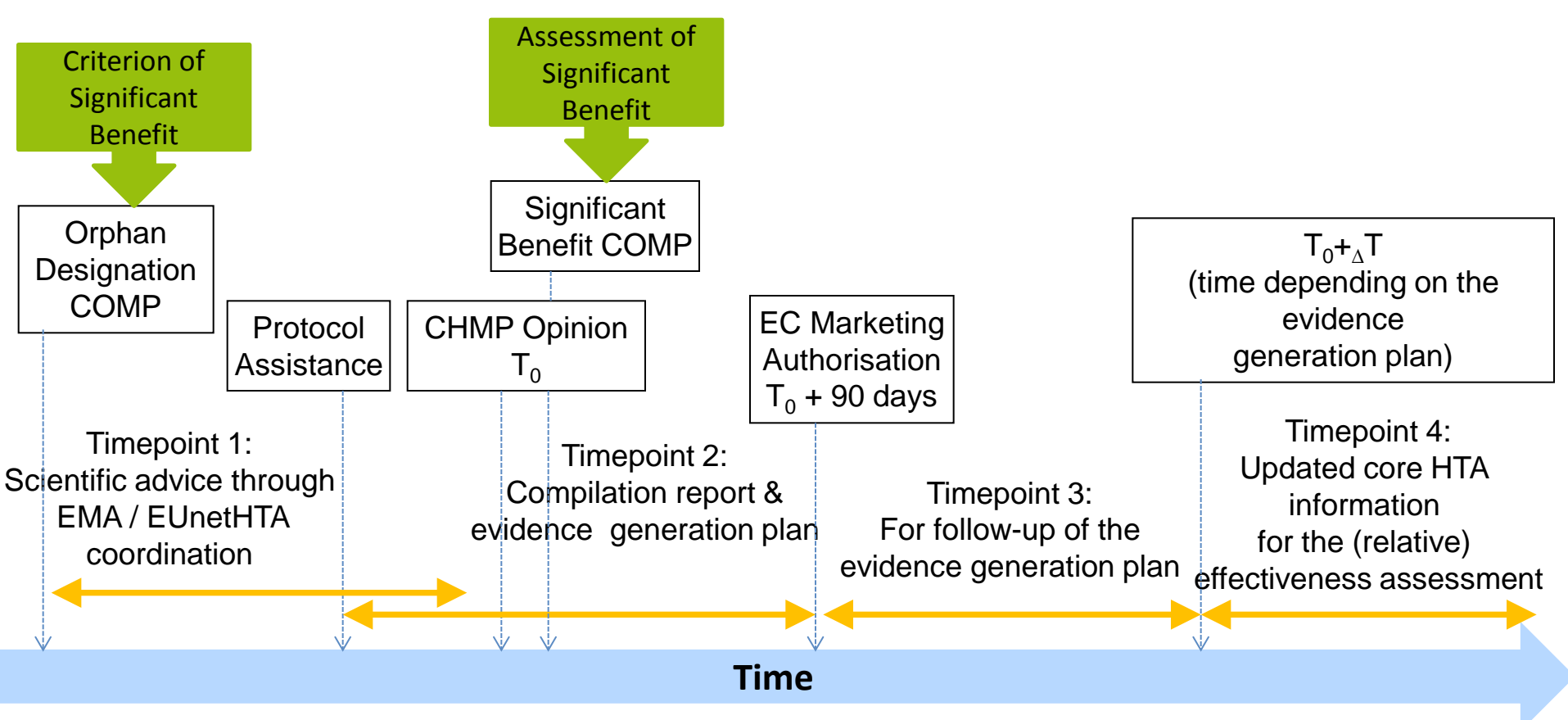
- **A current high priority for EURORDIS. Pilots in 2014?**

# Call for a Stronger FDA – EMA Collaboration: Beyond Orphan Drugs Designation

- **Coordinated Guidelines on the methodology of clinical trials & statistical methods per disease or relevant group of diseases**
- **Parallel Scientific Advice & Protocol Assistance**
- **Sharing of File, Mutual acceptance of data and Mutual Consultation on Assessment at time of MA**
- **Coordination of Post-MA research plans**

# CAVOMP: Four Time Points

1. **Early dialogue / Protocol Assistance**
2. **Compilation Report & evidence definition / Evidence Generation Plan**
3. **Follow-up of the evidence generation plan**
4. **Assessment of Relative Effectiveness**



Early Dialogue	Information exchange and defining the evidence generation plan	Evidence generation	Assessment
<ul style="list-style-type: none"> <li>EMA</li> <li>EUnetHTA / payers</li> <li>Sponsor</li> <li>Patients</li> <li>Experts</li> </ul>	<ul style="list-style-type: none"> <li>EMA</li> <li>EUnetHTA / payers</li> <li>Sponsor</li> <li>Patients &amp; treating physicians</li> </ul>	<ul style="list-style-type: none"> <li>EMA</li> <li>EUnetHTA / payers</li> <li>MAH</li> <li>Centres of Expertise (CE) &amp; European Reference Networks (ERNs)</li> </ul>	<ul style="list-style-type: none"> <li>EUnetHTA / payers</li> <li>EMA</li> <li>MAH</li> <li>Patients &amp; CEs/ERNs</li> </ul>
<ul style="list-style-type: none"> <li>Could be implemented already</li> </ul>	<ul style="list-style-type: none"> <li>Could be implemented already</li> </ul>	<ul style="list-style-type: none"> <li>Could be implemented already</li> </ul>	<ul style="list-style-type: none"> <li>Adapted methodological tools for OMPs to be developed</li> </ul>



# MOCA

- **A Mechanism for Coordinated Access to Orphan Medicinal Products – Corporate Responsibility Pharmaceuticals**
- **Consensus: A European Transparent Value Framework**
- **Ongoing: Pilots** between volunteering EU Member States and volunteering companies to discuss the Value
- **Opportunity: Price negotiation at European level based on Value (Common Assessment) + Volume (prevalence of therapeutic indication as defined in MA) + agreed Post-MA Research Activities – linking the 3 elements**

# Pan-European Managed Entry Agreements

- **Managed Entry Agreement is an area of active ongoing collaboration between EU Member States & Stakeholders – Corporate Responsibility Pharmaceuticals**
- **Consensus: the utility of such Managed Entry Agreements for new treatments targeted at small populations – rare diseases or stratified populations**
- **Ongoing: building consensus on concept, terminology, approaches**
- **Opportunity: Managed Entry Agreements linked to Patients Progressive Access / Adaptive Licencing and to negotiations through MOCA**

# Differential Pricing

- **Differential pricing is already a reality in today's OMP European market with variations of costs actually paid by MSs varying +/- 10%**
- **But these differences of prices have nothing to do with GDP or National Healthcare budget per capita**
- **Differential pricing is supported by a growing number of payers, industry, patient groups and policy makers**
- **Differential pricing for OMP can become a reality if associated with the negotiated / agreed price at European level - MOCA**

# National Measures in RD National Plans /Strategies

- **EU legislation & European Volunteering collaborative approaches can work only if well "appropriated" by Member States and "translated" into national measures"**
- **National Plans / Strategies on Rare Diseases are an opportunity to embed these measures in Member States' policy and organisation**

# CONCLUSIONS

## EURORDIS' Expectations

- **Parallel Scientific Advice /Protocol Assistance – HTA: More, Earlier, Better**
- **Guidelines: Anticipate, Align, Involve**

# Parallel SA/PA - HTA: More, Earlier, Better

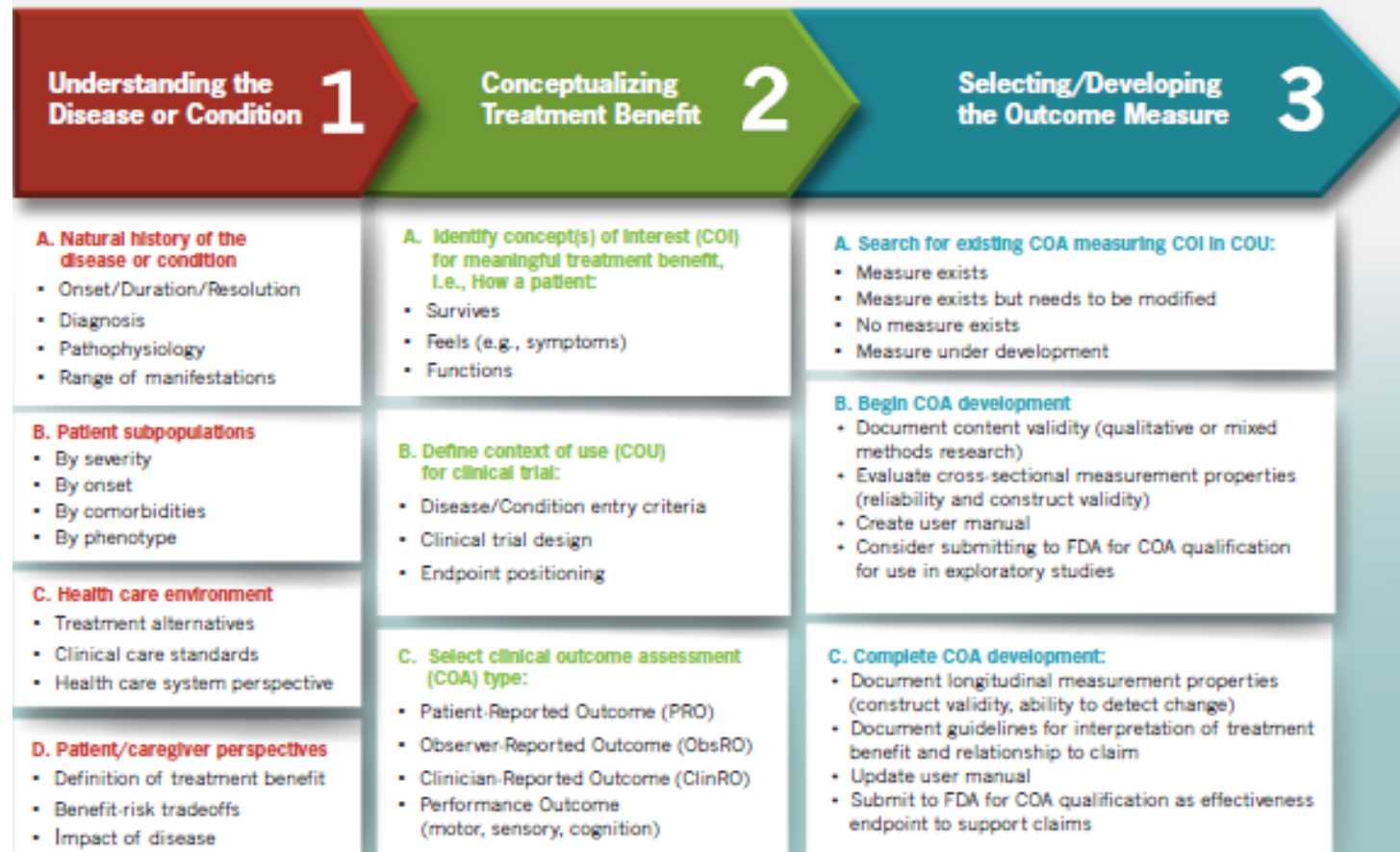
- **Continue and expand the EMA-HTA Parallel Scientific Advice**
- **Be more integrated – EMA-EUnetHTA**
- **Involve patients as experts not as observers + several patients ( a “must”) + with time to be prepared**

# Guidelines: Anticipate, Align, Involve

- **Promote more Guidelines on Clinical Trials on specific diseases or group of diseases:**
  - For diseases where there are several products coming up, several designation, some market authorisation (clusters)
  - Including Patients Focused Outcome Measures (cf EMA experience on its workshops and Guidelines or Points to Consider and the new FDA approach)
  - Jointly adopted EMA and EUnetHTA
- **Anticipate the development of these guidelines as early as possible as it take 12 to 18 months currently to draft, consult and adopt such guidelines**

# From the FDA

## Roadmap to **PATIENT-FOCUSED OUTCOME MEASUREMENT** in Clinical Trials





# Development of more OMPs requires more Europe

- **Encourage sponsors of designated orphan medicinal products to trigger this parallel procedure**
- **Parallel SA / PA educate both EMA and HTA to specificities of conditions not well known by them and for which only limited knowledge exist**
- **Flexibility and involve patients in risks appreciation**
- **For rare diseases, the only “competent level is Europe**

# THANK YOU



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