



EURORDIS
Rare Diseases Europe

RARE CANCERS CONSENSUS MEETING AND CONFERENCE

Improving the Methodology of Clinical Research on Rare Cancers

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**« SIGNIFICANT BENEFIT and
CLINICAL ADDED VALUE
IN THE CONTEXT OF ACCESS
TO ORPHAN DRUGS »**

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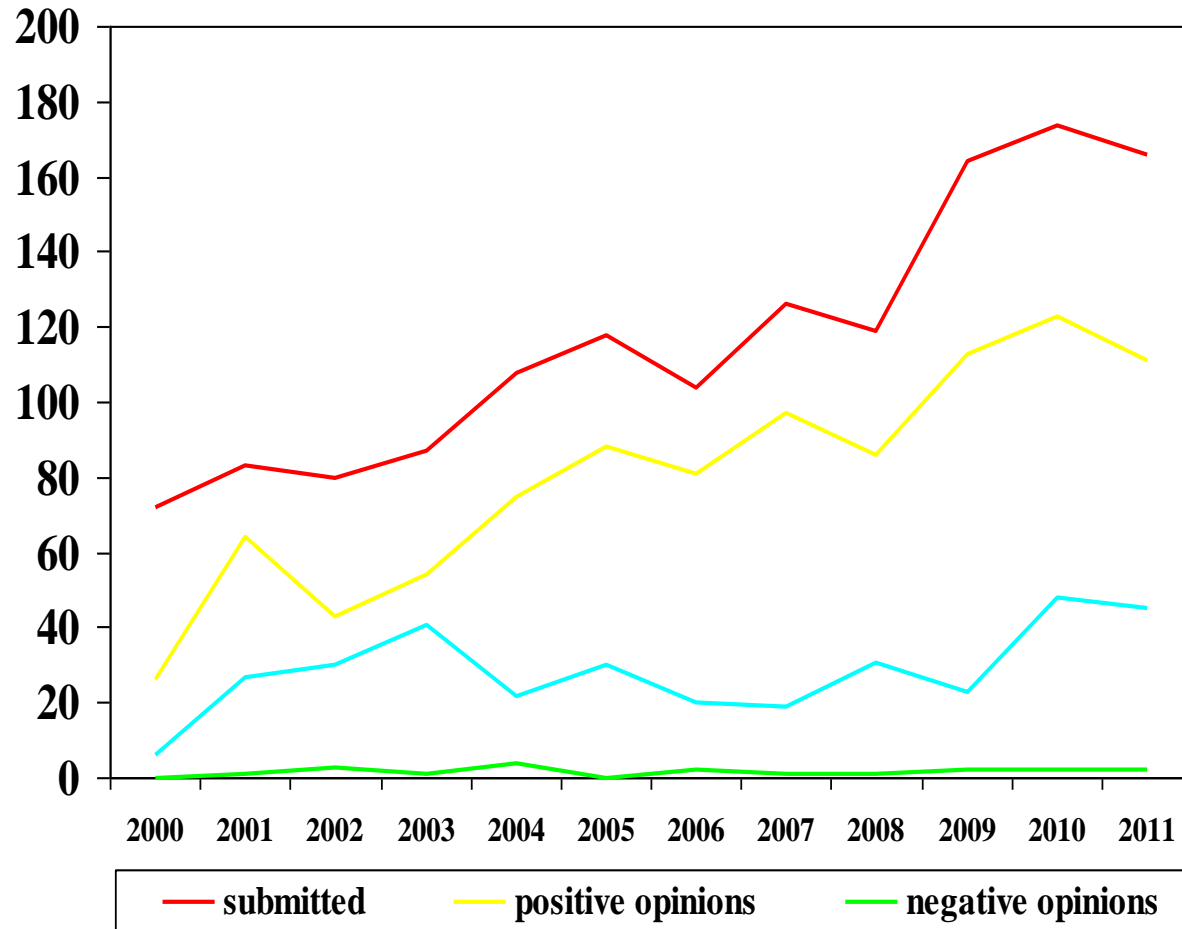
PART 1

ORPHAN DRUGS

&

RARE CANCERS

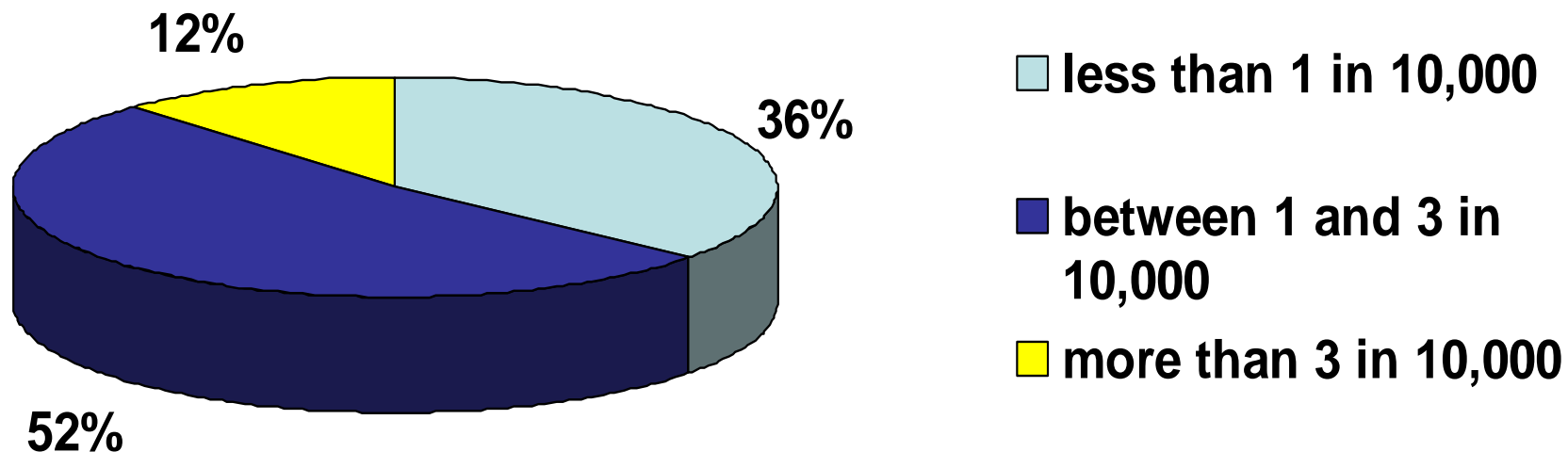
Outcome of orphan designation



**Success
rate of
designation
~70%**

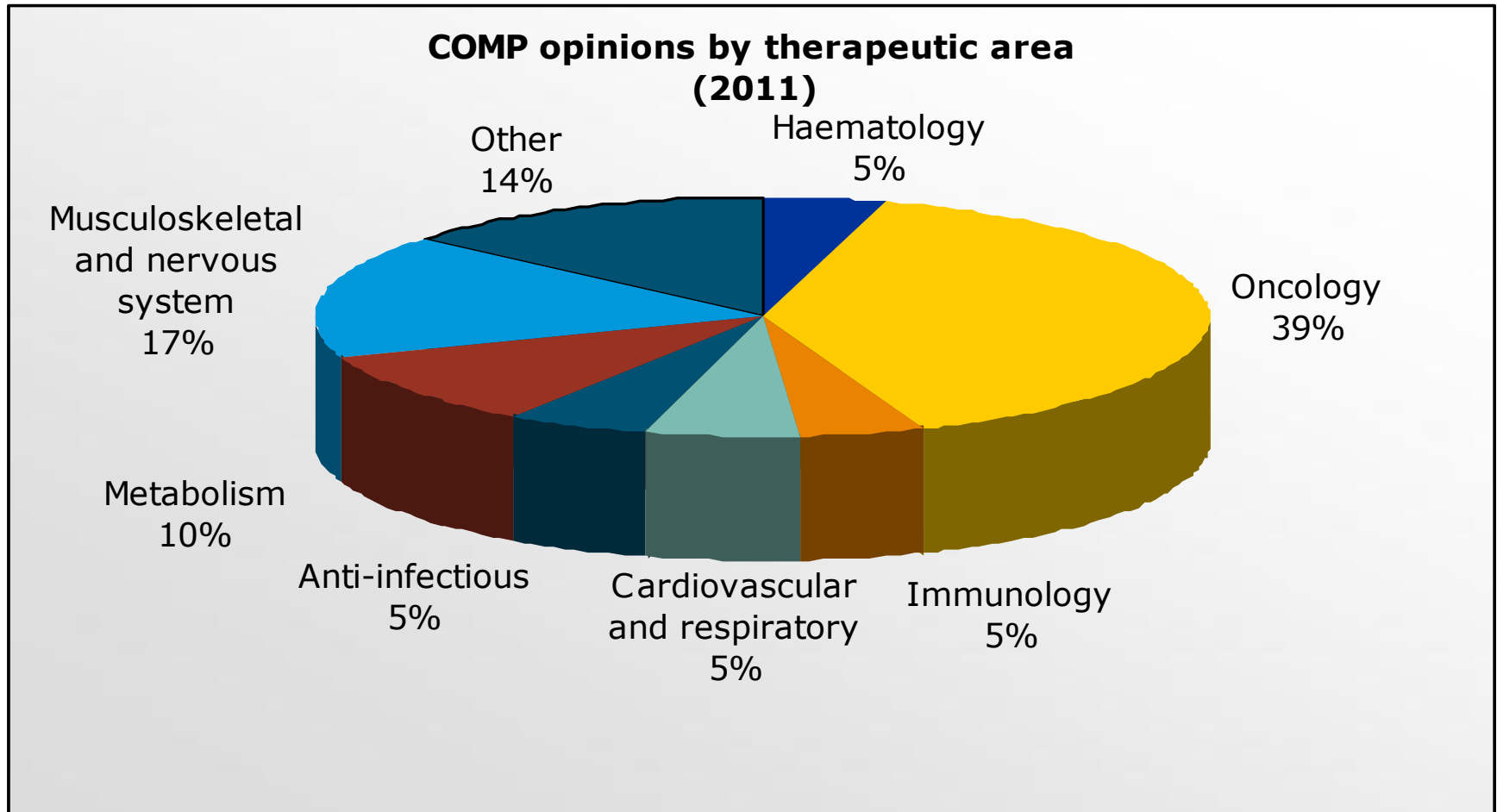
Source EMA COMP

Orphan Designations and Prevalence



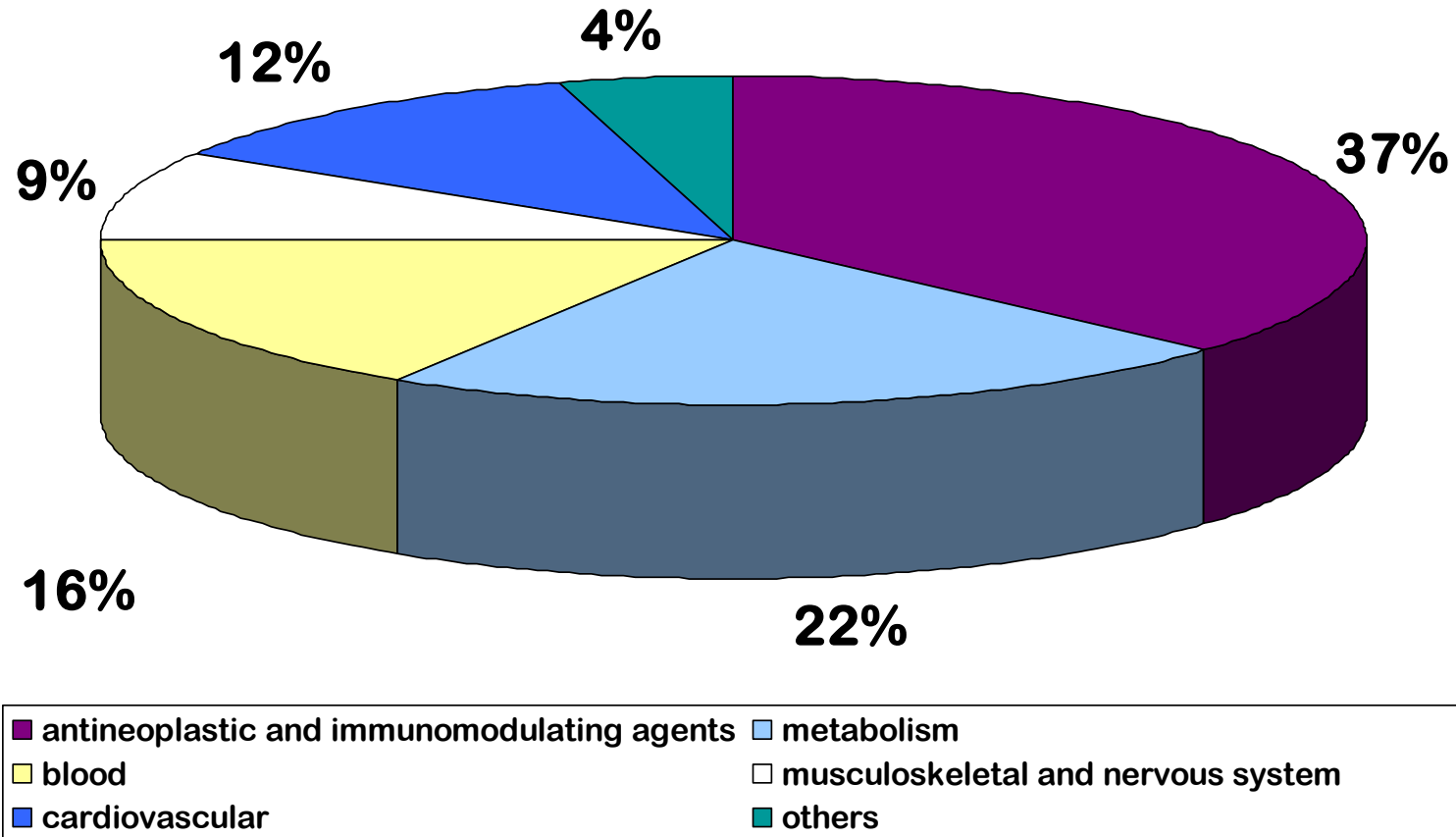
Source EMA COMP

Orphan Designation by therapeutic area



Source EMA COMP

Orphan products authorised per therapeutic area (n=69)



Source EMA COMP

Significant Benefit (SB) at time of MA

- **When COMP is reviewing the designation criteria :**
 - Over 60% of all orphan are designated including the criteria of potential significant benefit
 - In 2011, out of 7 MA for ODs, 4 were approved and maintained as OD and 3 lost their OD status but were still approved, due to lack of demonstration of Significant Benefit
- **Regulatory routes of approval of ODs & implications for SB:**
 - Standard or accelerated assessment in the case of unmet medical needs: 56% of MA for ODs
 - Conditional marketing authorisation : 38% of MA for ODs
 - MA under exceptional circumstances :6% of MA for ODs

PART 2

THE IMPORTANCE OF SIGNIFICANT BENEFIT FOR HTA, PAYERS AND PHYSICIANS

INTRODUCTION

**SIGNIFICANT BENEFIT IS A REAL ASSET
OF THE EU OD REGULATION AND
A POWERFUL TOOL OF COMP-EMA:
DIRECT IMPACT ON OD STATUS and
MARKET EXCLUSIVITY**

SIGNIFICANT BENEFIT IS IMPORTANT

- To stimulate the development of new orphan drugs, providing a medical benefit meaningful to patients, « a relevant relevant advantage» or «major contribution to patient care » for rare conditions over existing methods of treatment (or prevention or diagnostic)
- A measure to incentivise and channel investment into products bringing value to society
- A virtuous circle for the development of ODs

WHO KNOWS ABOUT SIGNIFICANT BENEFIT?

The importance of spreading the word and of speaking the same language

- Most HTA and Payers in Member States don't know a) that Significant Benefit exists, b) that it is specific to orphan drugs and meaningful for them, c) what it is...
- We need to have a **clear concept of Significant Benefit & clear assessment method** so that MSs end users could see what is the value of Significant Benefit **AND** as important: we **need to communicate about it!**

THREE MILESTONES OF SB

- At the time of OD Designation
- At the time of Protocol Assistance
- At the time of Marketing Authorisation

IMPORTANCE OF PUBLIC COMMUNICATION

The new Summary of COMP's Review of Criteria is a good improvement but...

- **COMP's Significant Benefit Assessment Reports should – in the future - be included in the same document as EPARs (tbc)**
- Write the reports so to be understood by HTA and payers. Could be part of the collaboration between EMA-EUnetHTA

THERAPEUTIC INDICATION as defined by CHMP IS IMPORTANT

- Condition & Updated description of the more specific medical condition targeted by the therapeutic indication → An essential point for patients, doctors and payers to address the high heterogeneity of the patient population for a given rare condition
- Prevalence & Updated data on the potential specific prevalence of the population targeted by the therapeutic indication → An essential point for the payers. An essential point to provide a reasonable and solid scientific argument to address the current fears and misperceptions on the costs of orphan drugs for society.

WORDS and CONCEPTS have changed in 15 years

SIGNIFICANT BENEFIT

AND

RELATIVE EFFICACY:

TWO SIDES OF THE SAME COIN!

PART 3

THE NEW IMPORTANCE OF EC INITIATIVES TO IMPROVE ACCESS TO ORPHAN DRUGS

TWO ONGOING INNOVATIVE APPROACHES TO IMPROVE ACCESS TO ORPHAN DRUGS

- ⇒ **Coordinated approach at EU level**

- **CAVOD**: a process to generate better data at time of MA and for post-MA research activities to assess the Clinical Added Value of Orphan Drugs (real life value, not clinical trial value) and the actual place of the product within the therapeutic strategy of the disease
- **MOCA**: Mechanism of Coordinated Access to Orphan Drugs between Member States, based on value, volume, access, generation of knowledge

Overall new paradigmes

- Focus on Effectiveness beyond Quality, Safety, Efficacy
Adapt Clinical Trial designs, as early as possible
Adapt Post MA Research plan

- Better and broader collection of relevant data

Data collected all along the life cycle of the medicine
on risks as well as on benefits: compassionate use,
real life studies (actual heterogeneous population and
real life constraints beyond clinical trials), off label use

Development of harmonised patient registries

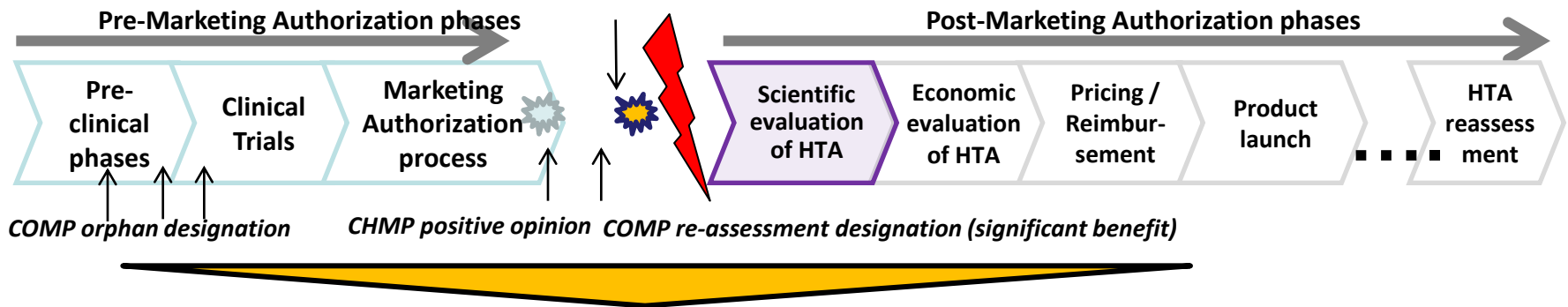
Common Assessment Reports on the Clinical Added Value of Orphan Drugs

- Scientific data from COMP, CHMP, PDCO + Post MA
- Written in a helpful way to identify the potential place of the new product in the therapeutic strategy of the rare condition, compared to existing treatment methods
- Regularly updated (3 to 5 years after MA) , based on data generated after the initial marketing authorisation, to identify the real place of the product, in the real life of medical practice and care, in the therapeutic strategy of the rare condition

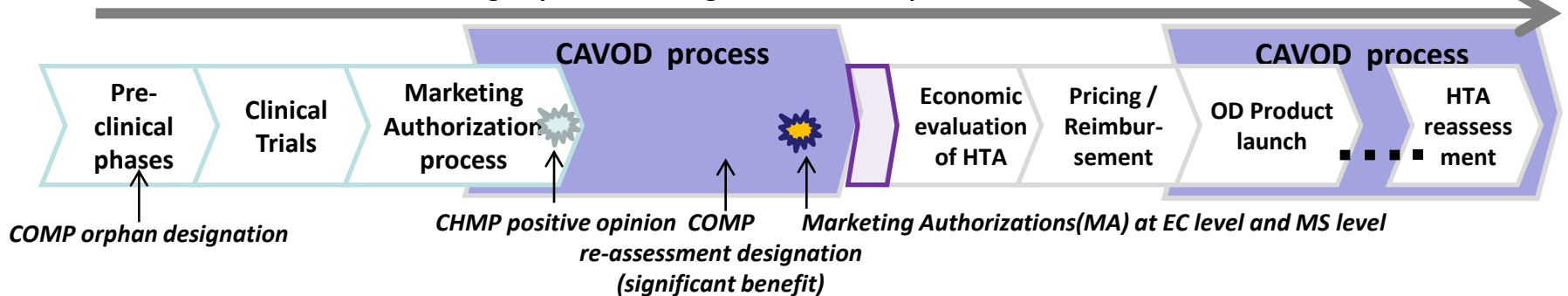
POSITIONNING OF THE CAVOD PROCESS

- The CAVOD process will contribute to make a bridge and develop a continuum between pre-market authorization practices (clinical development) at EU level and post-marketing authorizations practices at member state level:

Marketing Authorization (MA)



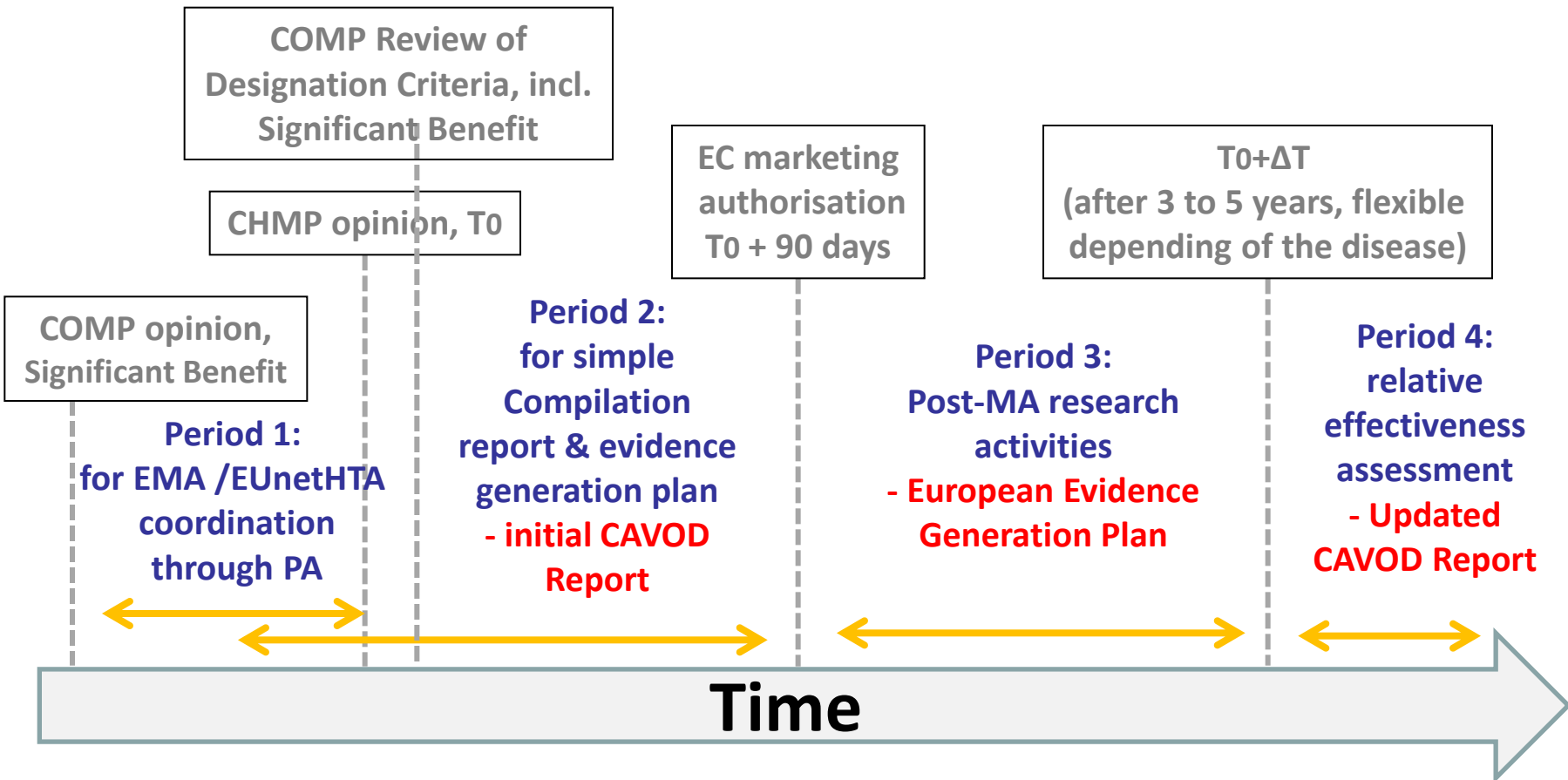
Pre-Marketing & post-Marketing Authorizations' phases



- The CAVOD mechanism should also help bridge the gap between regulators and HTA bodies

Source: Ernst & Young; Executive Agency for Health & Consumers

VISION AND ACTION: CAVOD MECHANISM



Source: Ernst & Young; Executive Agency for Health & Consumers

CAVOD TIMELINES

- Position Papers EURORDIS & EBE–EFPIA- EUROPABIO, (2009)
- ERTC Workshops on CAVOD (11 December 2009, 27 May 2011)
- EC/EAHC/ Ernst & Young Final Study Report on Mechanism to implement CAVOD (October 2011)
- EUCERD: Synthesis of CAVOD Report (January 2012)
- EUCERD Business Meeting on CAVOD March-April 2012
- EUCERD Recommendation on CAVOD (June 2012)
- Implementation: Pilots + EMA + EUnetHTA Joint Action

Exemple of current discussions: Pricing Matrix (and relevant to Significant Benefit)

The concept of a Pricing Matrix taking into account several parameters - still to be further discussed and confirmed:

- Prevalence: ex: 250 000-25 000 in EU or 25 000 - 2 500 in EU or < 2 500 in EU)
- Existence of alternative therapy or unmet medical need (significant benefit)
- Relative Effectiveness: ex: Incremental or Major or Curative (not accurate levels in my view - minor, medium and high would be more appropriate; including relative effectiveness based on safety or efficacy or contribution to patient care, curative could go more with the previous parameter with unmet medical need or alternative therapy existing or curative)
- Treatment Response Rate: ex: <30% or 30-60% or > 60%
- Degree of Certainty: ex: Promising but not Well Documented or Plausible or Unequivocal
- Pharmacoeconomic impact

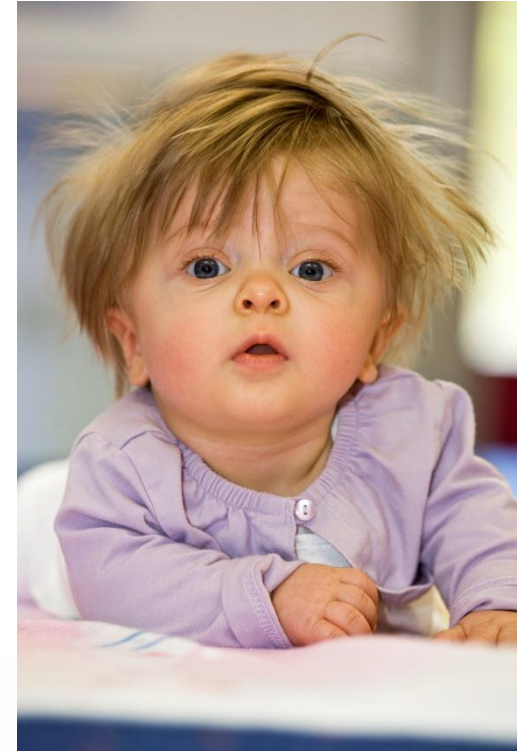
 = provided by COMP

 = provided by CHMP

CONCLUSION & WORKING PROPOSALS

- Significant benefit is important to HTA, Payers, Doctors
- Significant benefit, today, is in the context of Relative Efficacy, Relative Effectiveness, Clinical Added Value Assessment based on knowledge generated, and, Reimbursement & Real Patient Access based on Value

THANK YOU !



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