EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Update of CHMP Guideline on Conditional marketing authorisation (CMA)

Overview of changes proposed and comments received during public consultation

Presented by Sonia Ribeiro on 20 October 2015 at 3rd STAMP meeting
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Human Medicines Research and Development Support Division

# Overview

- Experience with CMA presented at 1st STAMP meeting
- CHMP Considerations on CMA presented at 2nd STAMP meeting
- Updated guideline released for public consultation in July 2015
- Comments due date 30 September 2015
- Discussion on CMA at 3rd STAMP meeting

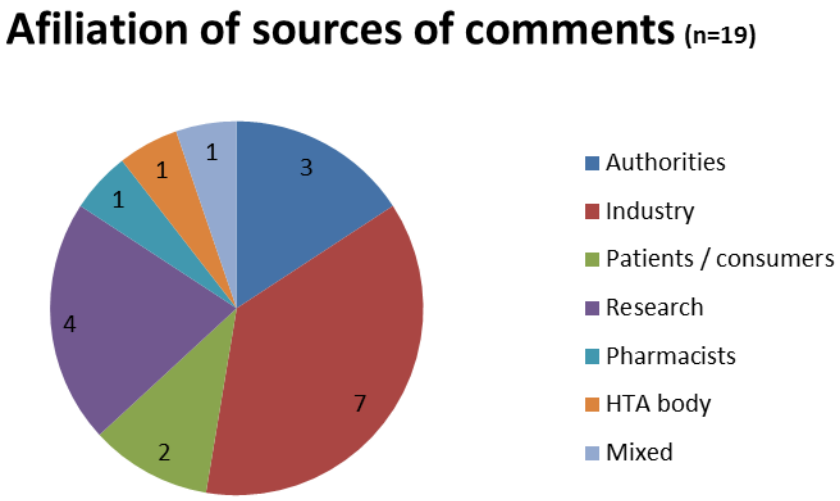
# Changes to the Guideline for public consultation (I)

- Encouragement of early dialogue and **prospective planning**;
- Requirement of '**positive benefit-risk balance**':
  - Clarification on benefit-risk balance in case of non-comprehensive data;
  - Include examples and further guidance on the level of evidence required at the time of authorisation (e.g. use of intermediate endpoints that are reasonably likely to translate into clinical benefit) and the data that can be provided post-authorisation through specific obligations (SOs).
- Exceptionally, **improvements in patient care** as a possible major therapeutic advantage, in addition to better safety and/or efficacy;
- Serious debilitation and life-threatening effects also in the **long-term**.

# Changes to the Guideline for public consultation (II)

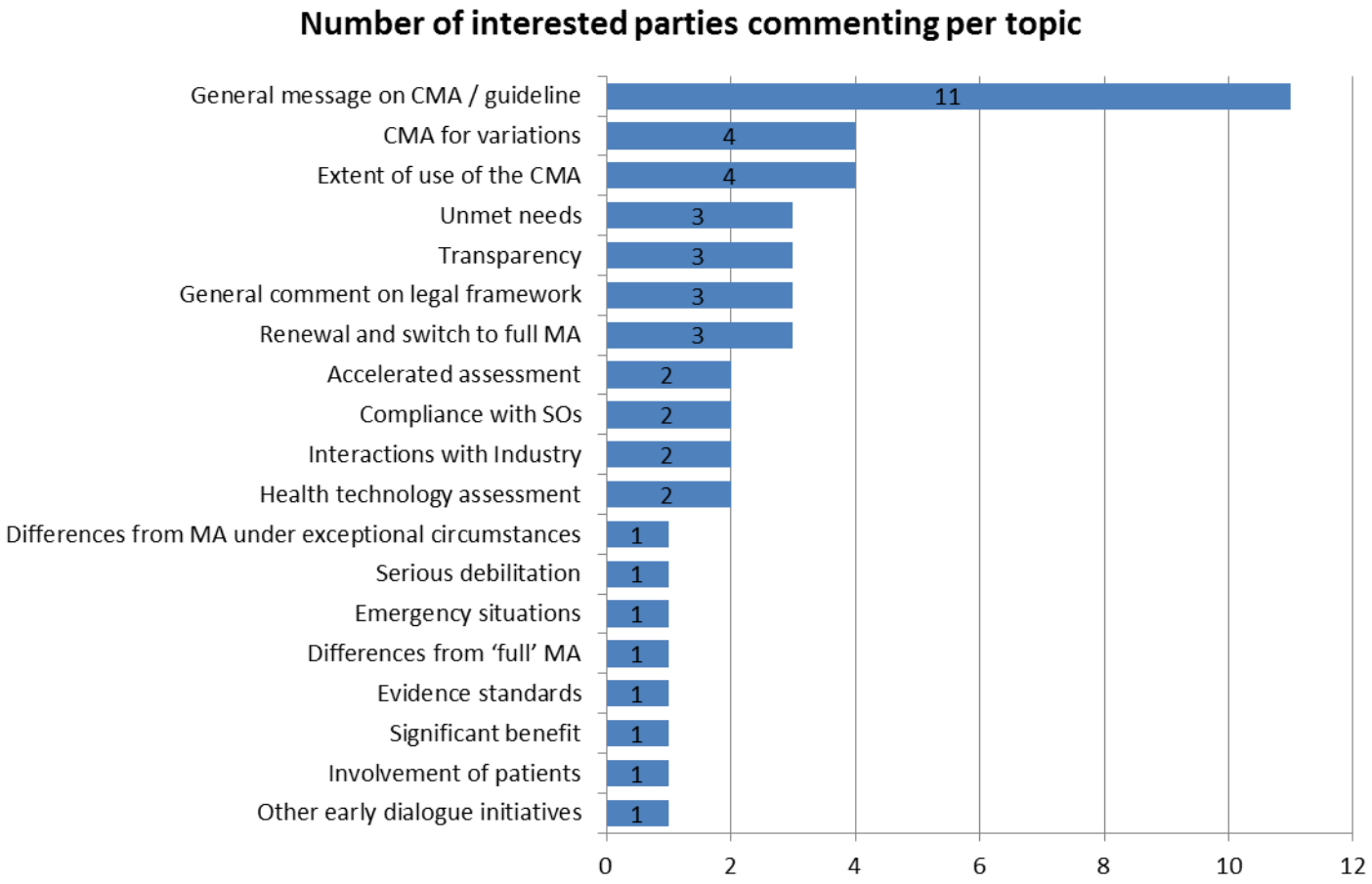
- Confirmation of **significant benefit for orphan medicinal products** – need to consider data required as part of prospective planning of CMA, cooperation with COMP reflected at high level in the guideline
- Amendment and expansion of wording in several parts **to better reflect what products can be suitable for CMA**
- Clarifications on some further aspects (e.g. on products to be used in emergencies, compatibility with **accelerated assessment**, submission of data in **annual renewals**)

# Sources of comments received

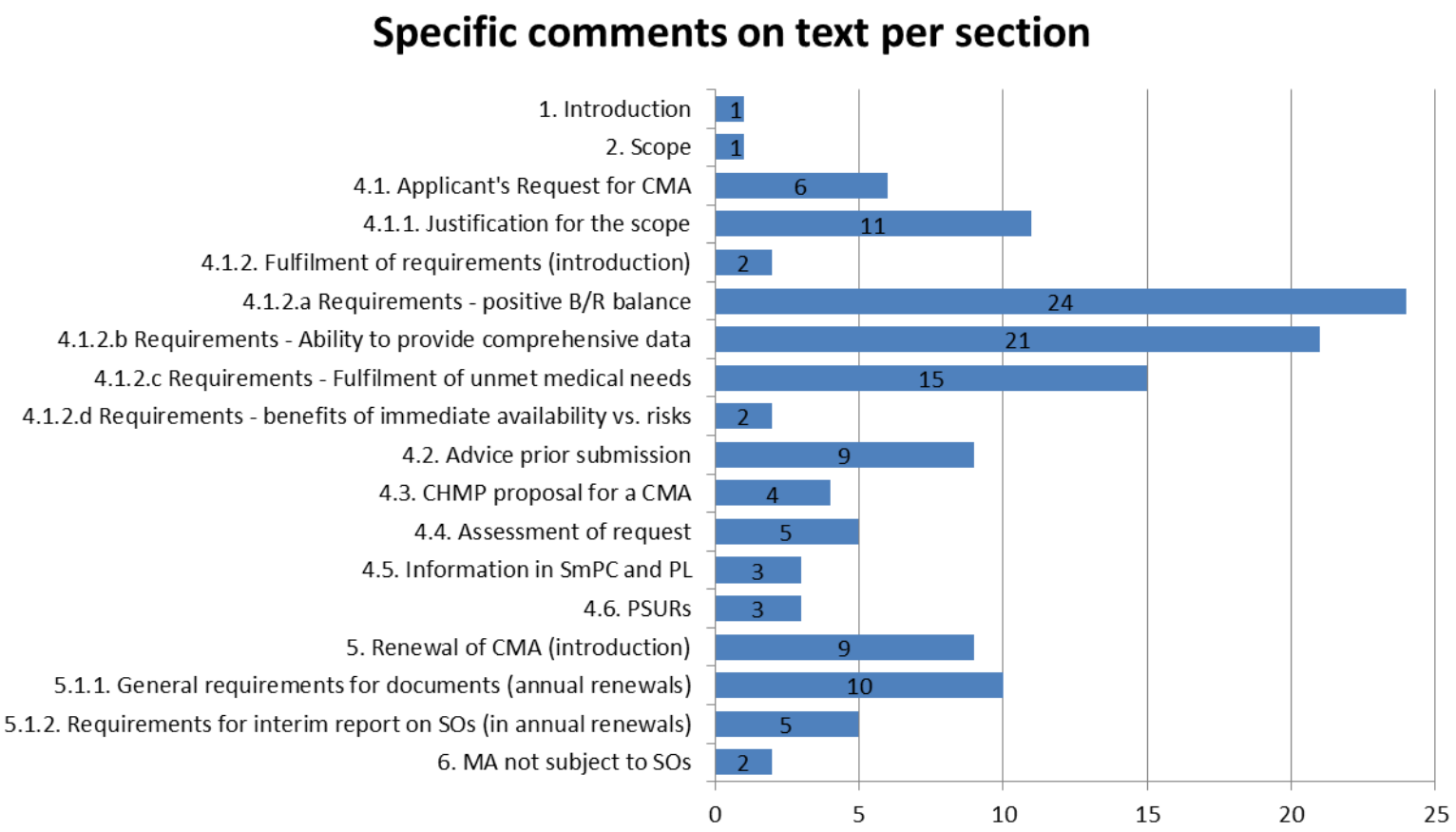



| |
|---|
| Alexion Pharma GmbH |
| ANSM (French Health products Safety Agency) – Evaluation Division |
| BEUC – The European Consumer Organisation |
| BIO Deutschland e.V. – the German Biotech Industry Association |
| Cancer Research UK |
| Centre for Health Technology Evaluation, National Institute for Health and Care Excellence (NICE) |
| EFPIA - European Federation of Pharmaceutical Industries and Associations |
| EORTC: European Organisation for Research and Treatment of Cancer |
| EuropaBio - the European Association for Bioindustries |
| European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) |
| European Organisation for Rare Diseases (EURORDIS) |
| Health Action International (HAI), the International Society of Drug Bulletins (ISDB) and Medicines in Europe Forum (MiEF) |
| IABS-EU as a member of the IMI – Zoonoses Anticipation and Preparedness Initiative |
| International Plasma Fractionation Association (IPFA) |
| Norwegian Medicines Authority (NOMA) |
| Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel (Federal Institute for Vaccines and Biomedicines) |
| Pharmaceutical Group Of the European Union (PGEU) |
| REGenableMED consortium (REGenableMED is a United Kingdom Economic and Social Research Council (ESRC)-funded project) |
| Teva Pharmaceutical Industries Ltd |

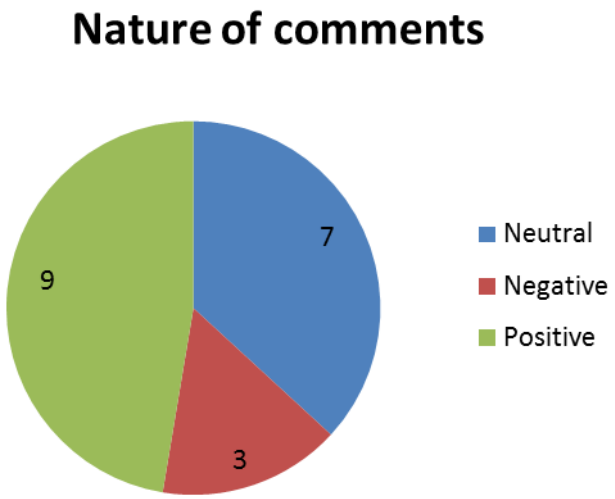
# Topics of General comments

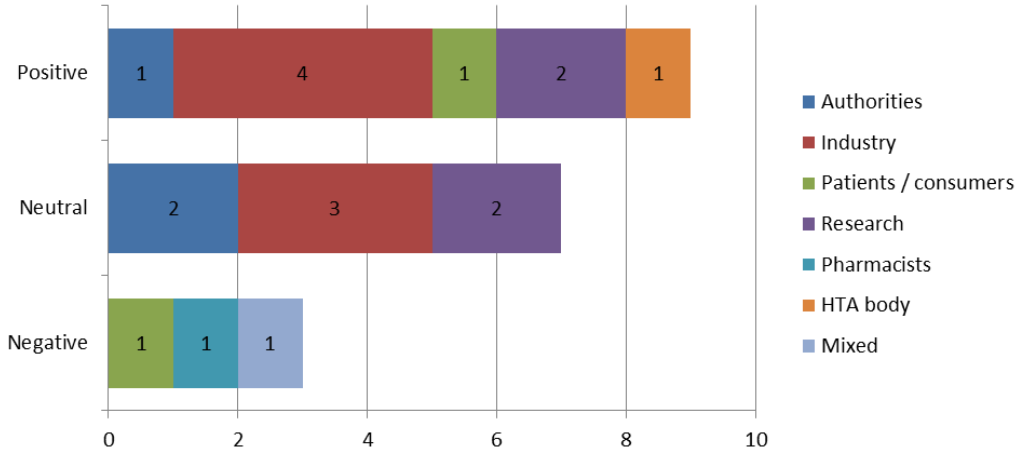


# Comments on the text of the guideline



# Perception of the Guideline update



# Examples of comments received

**General**

We welcome that the revised guidance emphasises the importance of early dialogue with the EMA. Such an approach gives the organisations developing new treatments more certainty about the approach they take to gathering evidence and how it will be treated during assessment.
Cancer Research UK

It is important that the CMA procedure is used and seen in a positive manner.
EUCOPE

We support and appreciate the proposed changes. NOMA

**Extent of use of CMA**

The importance of maintaining the requirement for solid evidence about benefits and harms before a medicine is approved as the corner stone of pharmaceutical regulation must be emphasised. HAI-ISDB-MiEF

These "expedited" schemes are legitimate when there is a real unmet health need. HAI-ISDB-MiEF

The relatively small number of CMAs indicates a revision to the guidance is needed in particular to increase the applicability in the oncology field and beyond. EFPIA

# Examples of comments received

**Other topics**

Licensing under emergency use requires extremely flexible approaches. IABS-EU

A general comment would be to provide more information on these discussions, particularly for products benefiting from a long-lasting conditional authorisation where the public may question why it seems so difficult to fulfil the post-marketing obligations. EURORDIS

The cooperation between CHMP and COMP in their assessments is seen as a positive new process. EUCOPE

EFPIA also welcomes the renewed interpretation for evidence generation in demonstrating benefit/risk in order to obtain CMA (lines 120-123) while strengthening the criteria for the MAH to fulfil the specific obligations (lines 339-342). EFPIA

[..] request to reduce the requirements for an annual renewal and only include these items which have changed and are critical to assess that the MAH is fulfilling its commitments. EFPIA

# Selected comments for STAMP discussions

## Legal Framework

### CMA should be allowed for **extensions of indications**

This would also limit off label use of the approved product for a not yet approved indication. (Alexion Pharma)

The previous paragraph that stated that CMAs do not apply to new indications has been removed. We would welcome confirmation that this implies that CMAs can now be applied to new indications and line extensions. (EFPIA)

Suggested by EFPIA, Alexion Pharma, EuropaBio, Teva

### Other comments

It would be welcomed when comparable approaches **for veterinary medicinal products** would be available as well. (IABS-EU)

For all categories within the scope of Article 2 of the commented Draft Guideline a conditional marketing authorisation should be **possibly granted with less preclinical, pharmaceutical** and/or clinical **data**. (BIO Deutchland)

# Selected comments for STAMP discussions

## Unmet medical need

The concept of "innovative medicines" shall be understood to refer to medicines that meet true unmet medical needs. The criteria for granting marketing authorisation for medicines should move towards an approach where **comparative-trials against the best available treatment** are requested and the question of the added therapeutic value is a determining factor in granting approval. (HAI-ISDB-MiEF)

Situation when conditional approval could be granted: in case a **long-lasting shortage** has occurred for an authorised medicine and another one is being evaluated for the same indication (cf Fabrazyme and Cerezyme shortages for example) (EURORDIS)

Once unmet medical need has been confirmed for a product and CMA has been obtained for molecules of the same class and same indication, the **"unmet medical need" should not be considered to have been met as long as the status of the first product is still conditional**. (EFPIA)

When considering the public health importance of these medicines, which is one of the explanations for this regulatory route being made available, it is vital that further precision is provided on what justification is required to demonstrate **'public health unmet need'** [..]. We note that this is not included in the legal provisions. (NICE)

# Selected comments for STAMP discussions

## Compliance with specific obligations

In contrast to the approach proposed by the EMA in its consultation document, concrete measures to dissuade, penalties and sanctions should be applied to those marketing authorisation holders which do not comply with their obligations. The EMA must closely monitor marketing authorisation holders and **apply sanctions** in case of non-compliance (i.e. in the form of fines; removal of conditional approval). (HAI-ISDB-MiEF)

EFPIA also **welcomes** the renewed interpretation for evidence generation in demonstrating benefit/risk in order to obtain CMA (lines 120-123) while **strengthening the criteria for the MAH to fulfil the specific obligations** (lines 339-342). (EFPIA)

# Selected comments for STAMP discussions

## Involvement of HTA bodies

We support statements in the documents about the need to consult with other stakeholders. We suggest that these statements are further strengthened throughout the document as **engagement with those responsible for downstream medicines access policy is crucial to the successful implementation of regulatory early access procedures**.

We strongly suggest that regulatory approval under early access should include provisions for **data generation that have been agreed via multi-stakeholder dialogue**.

The EMA might go as far as to indicate that evidence of this type of engagement [with HTA bodies] would be taken into account when assessing to what extent the company has provided sufficient justification with respect to plans for post-regulatory approval evidence generation.

(NICE)

# Selected comments for STAMP discussions

## Accelerated assessment

A product which fulfils the unmet medical need criterion for an application for a conditional marketing authorisation could be viewed as **automatically** falling under the criterion of 'major interest from the point of view of public health and from the point of therapeutic innovation' allowing a request for an **accelerated assessment** procedure. (EFPIA)

# Next Steps

- Discussions on public consultation comments and input from the STAMP with CHMP sponsors and committees
- Consultation with the EC to obtain favourable opinion
- Adoption of the final guideline by the CHMP

# Thank you for your attention

## Further information

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