EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

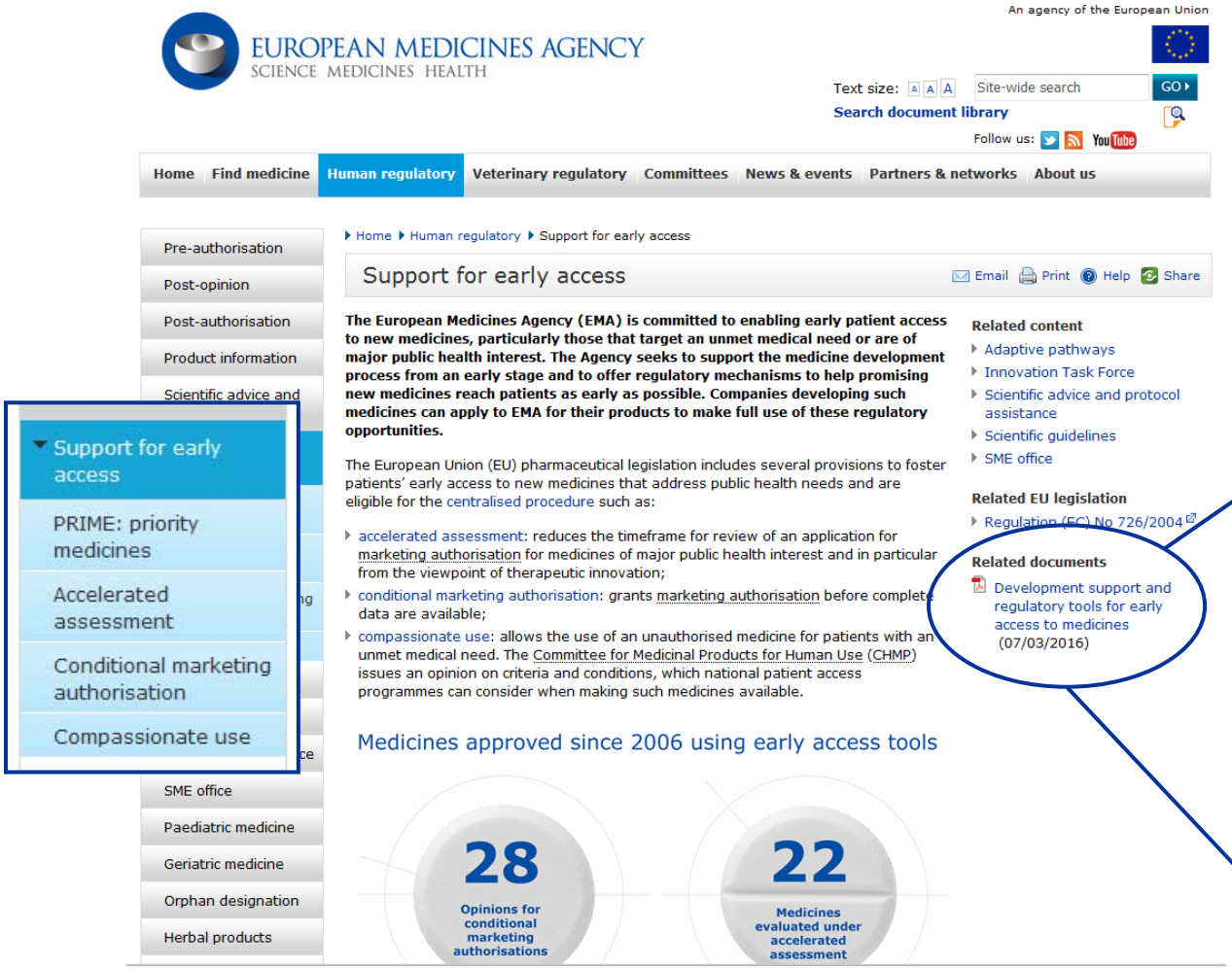
Update on PRIME and CHMP Guidelines for early access tools

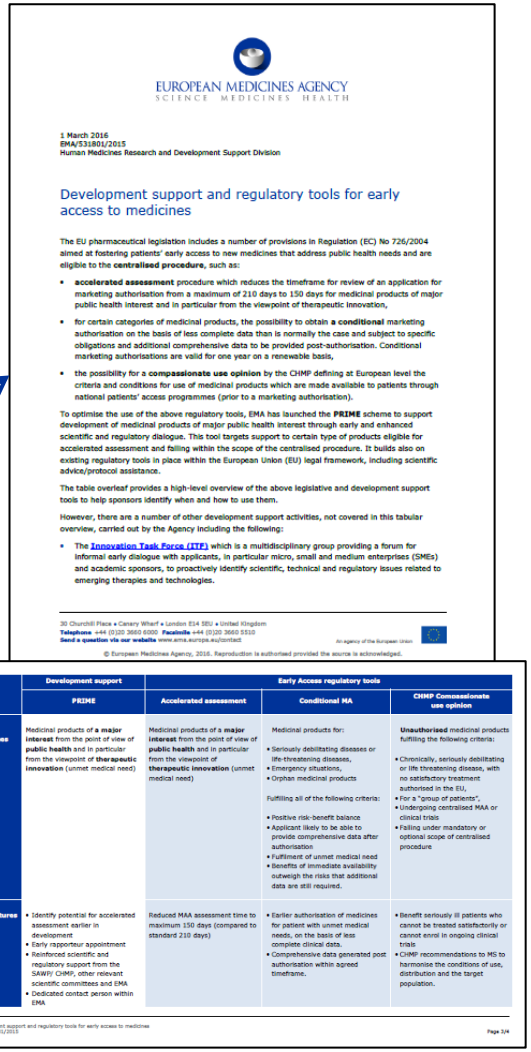
4th STAMP meeting, 10 March 2016

Presented by Zaide Frias
Human Medicines Research and Development Support Division

An agency of the European Union

Launch of PRIME and updated guidelines





http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000856.jsp&mid=WC0b01ac058096f643

1 Update on PRIME and CHMP Guidelines for early access tools

PRIME

After discussions at all STAMP 2015 meetings

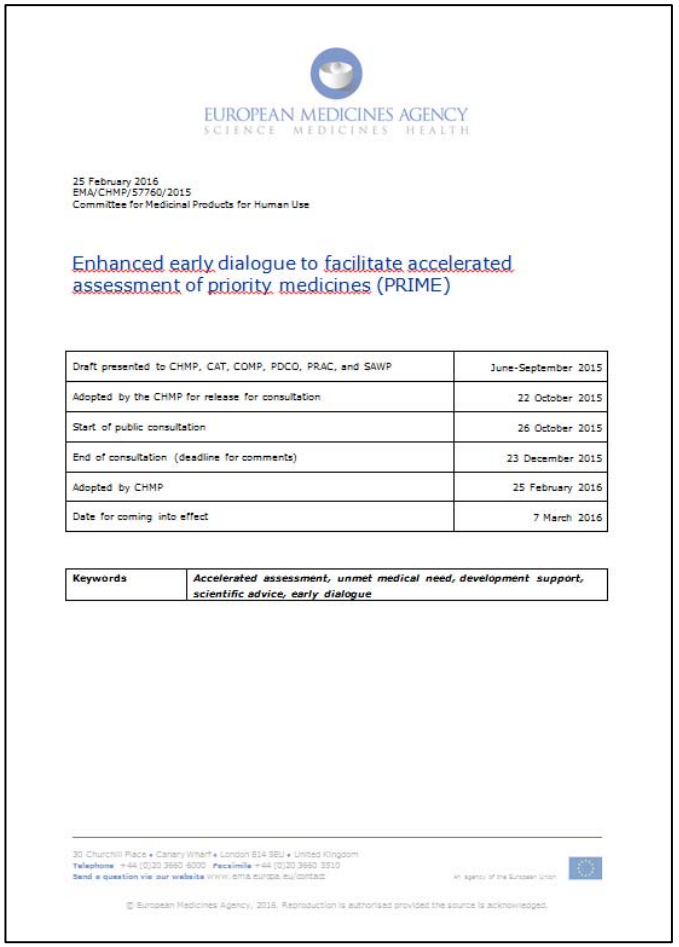
Draft reflection paper adopted by CHMP

Public consultation

Review of comments and revision of the document

Finalisation and adoption of the document

Scheme launched on 7 March



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/57760/2015
Committee for Medicinal Products for Human Use

Enhanced early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

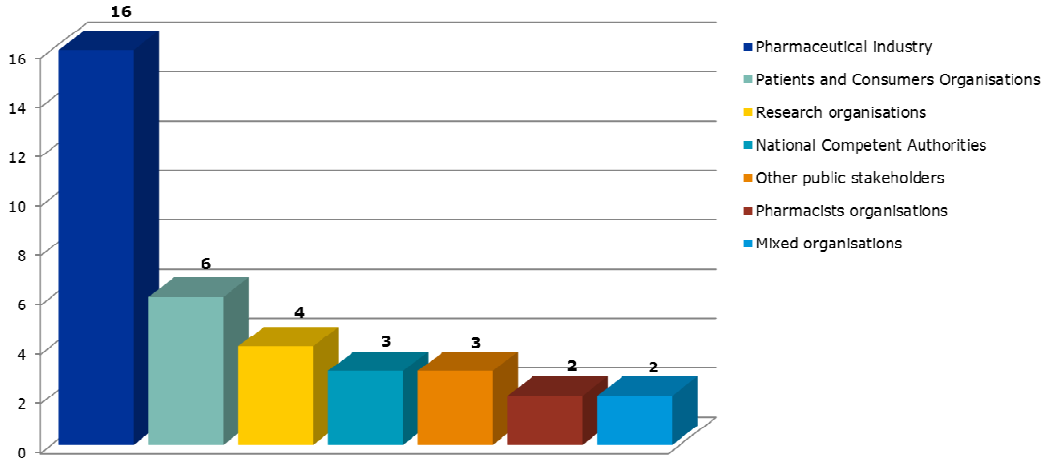
Draft presented to CHMP, CAT, COMP, PDCO, PRAC, and SAWP	June-September 2015
Adopted by the CHMP for release for consultation	22 October 2015
Start of public consultation	26 October 2015
End of consultation (deadline for comments)	23 December 2015
Adopted by CHMP	25 February 2016
Date for coming into effect	7 March 2016

Keywords	*Accelerated assessment, unmet medical need, development support, scientific advice, early dialogue*

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 Facsimile +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Public consultation on PRIME

- 36 contributions from 42 stakeholders
- Wide range of stakeholders
- > 300 comments
- All comments published on EMA website, together with summary and responses



PRIME - Main changes after public consultation (1)

Eligibility criteria - Clarifications and refinement of wording

3. PRIME Eligibility criteria

The PRIME scheme is limited to products under development which are innovative and yet to be placed on the EU market. There should be an intention to apply for its initial marketing authorisation through the centralised procedure.

The scheme aims to support medicinal products of **major public health interest** and in particular from the viewpoint of therapeutic innovation **(i.e. those which fulfil the accelerated assessment criteria)**.

As such, medicines eligible for PRIME support shall target conditions where there is an **unmet medical need**, i.e. for which there exists no satisfactory method of diagnosis, prevention or treatment in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

- In these conditions, a product eligible for PRIME support should demonstrate the **potential to address to a significant extent the unmet medical need** for maintaining and improving the health of the Community, for example, by introducing new methods of therapy or improving existing ones. Data available to support a request for eligibility in a given indication should support the claim that the product has the potential to bring a major therapeutic advantage to patients, through a clinically meaningful improvement of efficacy, such as having an impact on the prevention, onset or duration of the condition, or improving the morbidity or mortality of the disease.

The appropriateness for access to the PRIME scheme depends on both the magnitude of the treatment effect, which could include duration of the effect, and the relevance of the observed clinical outcome. Relevant clinical outcomes generally refer to an endpoint that predicts an effect on associated morbidity, mortality or progression of the underlying disease.

Consequently, entry to the scheme for the majority of products is expected to be supported by evidence of clinical response in patients (i.e. generated in exploratory clinical studies) substantiating the product's potential to significantly address the unmet medical need by providing a clinically relevant advantage for patients.

As the data submitted will vary depending on the product, stage of development and therapeutic area, each request will be considered on a case by case basis.

Detailed guidance on the justification to be submitted by applicants to be part of the scheme is provided in Annex 1.

Annex 1 – Justification for eligibility to PRIME

The request should be submitted with justification that the eligibility criteria are met in a given indication and should be presented as a short but comprehensive document (not more than 30 pages in length). The following aspects could be considered, as appropriate, in the justification:

Unmet medical need

- In general, the justification will be more convincing if based as much as possible on epidemiological data about the disease (e.g., life expectancy, symptoms and duration, health-related quality of life). The claims could be substantiated e.g., from published literature or registries or healthcare databases.
- Where relevant, the unmet medical need should be described separately for different indications or subpopulations.
- A description of the available diagnostic, prevention or treatment options/standard of care (SOC), including all relevant treatment modalities, e.g., medicinal products used in clinical practice (whether approved or not), devices, surgery, radiotherapy should be included. The effect of available methods should also be described together with a description of how the medical need is not fulfilled by the available methods.

Potential to significantly address the unmet medical need

- The extent to which the medicinal product is expected to address the unmet medical need (described in the above bullet point) is essential to its eligibility for PRIME support. The justification should include a description of the medicinal product's observed and predicted effects, their clinical relevance, the added value of the medicinal product and its impact on medical practice. It is noted that a new mechanism of action or a technical innovation *per se* may not necessarily represent a valid argument for justifying major interest from the point of view of public health.
- In case authorised treatments or established methods exist, the expected improvements should be discussed through a critical review comparing authorised or clinically established treatments and the proposed product.

PRIME - Main changes after public consultation (2)

Increased transparency

Publication of name of active substance/INN of eligible products

An overview of the number of recommendations adopted will be published in the CHMP Monthly report. The EMA will also publish information on products for which eligibility to the scheme has been granted, including the name of the active substance/INN, the type of product (chemical, biological or advanced therapy), the intended indication, the type of data supporting the eligibility request and the type of applicant (SMEs, applicants from the academic sector or others). For products that have been denied eligibility, similar information will be published, with the exception of the name of the active substance/INN, to avoid unintended negative connotations on the merit of the product at the early stage of its development. In case of a subsequent centralised marketing authorisation, reference to eligibility to the PRIME scheme and relevant information will be mentioned in the European Public Assessment Report.

PRIME - Main changes after public consultation (3)

Focus on SME and Academia

Clear acknowledgement of hurdles faced by SME and academia

Progressing to proof of concept stage is often a difficult step for smaller actors with limited experience in regulatory aspects and medicine development. This may hinder the development of promising products. Therefore, there is value in opening the scheme to SMEs and applicants from the academic sector at an earlier stage. This additional support is expected to be exceptional and limited to situations where earlier proof of principle/proof of mechanism stage (prior to, or during, early exploratory clinical studies) is supported by compelling data that can be presented to justify a product's potential public health impact.

Additional benefits of PRIME

Early regulatory support

Potential to help capital investment

Fee reductions

In early stages of development, following demonstrated proof of principle, focusing on SMEs and applicants from the academic sector:

- Raising awareness of regulatory requirements early in the development, by providing scientific and regulatory advice on the overall development plan and at major development milestones, with the possibility to involve multiple stakeholders (e.g. Health Technology Assessment (HTA) bodies, patients).
- Eligibility to PRIME may help these applicants to overcome financial hurdles[3] to progress through later stages of the development.
- Upon request, SMEs and applicants from the academic sector[4] may also be eligible for fee reductions on their scientific advice requests, upon case-by-case decisions.

PRIME - Main changes after public consultation (4)

New section to highlight importance of collaborations

Innovation offices

Role in raising awareness to PRIME, exchange of information

HTA

EMA to encourage use of relevant tools supporting early dialogue with HTAs

International cooperation

Global development context and confidentiality arrangements

7. Collaboration

Innovation offices exist in a number of EU Member States. These offices are in contact and support applicants in very early stages of developments. They will have an important role in raising awareness to PRIME and directing possible candidates towards the scheme. The Agency collaborates with the Innovation offices and will exchange information on the scheme and its output on a regular basis.

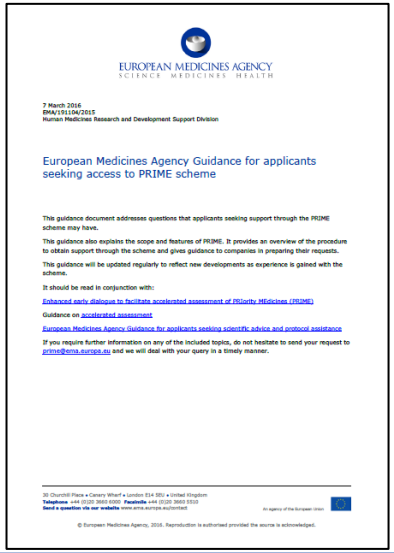
EMA is committed to facilitating as much as possible the assessment of priority medicines done by **health technology assessment (HTA) bodies,** which inform reimbursement decisions by Member States. This is vital so that patients can access new medicines in a timely manner. In the last years the Agency has launched various initiatives to strengthen collaboration with these bodies. In view of its aim to promote the possibility of earlier patients' access, as part of PRIME, EMA will encourage medicine developers to make use of relevant tools supporting early dialogue with HTAs, such as the parallel EMA/HTA advice.

The importance of considering PRIME in the context of global developments and **international cooperation** is acknowledged. As part of their confidentiality agreements, EMA and other agencies may exchange information on specific medicines' development and experience on development support tools.

PRIME webpage and supporting documents

Factsheet in lay language

Q&A, templates, application form for applicants



Update of CHMP Guidelines on accelerated assessment and conditional MA

Reflections on the experience

Drafting of guideline update

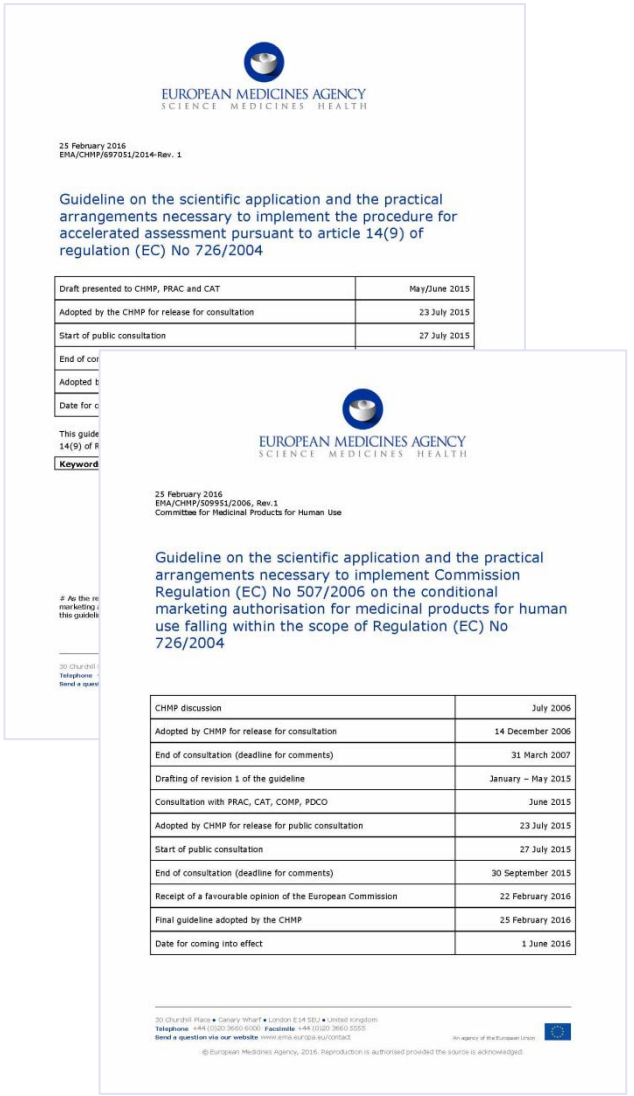
Consultation with other committees ★

Public consultation

Review of comments and revision of the guideline ★

Favourable opinion of the European Commission* ★

Finalisation and adoption of the guideline February 2016



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/697051/2014-Rev. 1

Guideline on the scientific application and the practical arrangements necessary to implement the procedure for accelerated assessment pursuant to article 14(9) of regulation (EC) No 726/2004

Draft presented to CHMP, PRAC and CAT	May/June 2015
Adopted by the CHMP for release for consultation	23 July 2015
Start of public consultation	27 July 2015
End of cor	
Adopted b	
Date for c	

This guide
14(9) of R

Keyword

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/509951/2006, Rev.1
Committee for Medicinal Products for Human Use

Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

CHMP discussion	July 2006
Adopted by CHMP for release for consultation	14 December 2006
End of consultation (deadline for comments)	31 March 2007
Drafting of revision 1 of the guideline	January – May 2015
Consultation with PRAC, CAT, COMP, PDCO	June 2015
Adopted by CHMP for release for public consultation	23 July 2015
Start of public consultation	27 July 2015
End of consultation (deadline for comments)	30 September 2015
Receipt of a favourable opinion of the European Commission	22 February 2016
Final guideline adopted by the CHMP	25 February 2016
Date for coming into effect	1 June 2016

* for CMA guideline only

★ Update provided to STAMP

Key changes to CHMP Guideline on conditional MA

- Encouragement of early dialogue and **prospective planning**
- '**Positive benefit-risk balance**' vs. comprehensive dossier
- Scope of CMA to cover serious debilitation and life-threatening effects also in the **long-term**
- Exceptionally, **improvements in patient care** as a possible major therapeutic advantage
- Guidance on situations when a **second product** can still address the same unmet medical need
- Confirmation of **significant benefit for orphan medicinal products**
- Clarifications on some further aspects (e.g. compatibility with **accelerated assessment**)

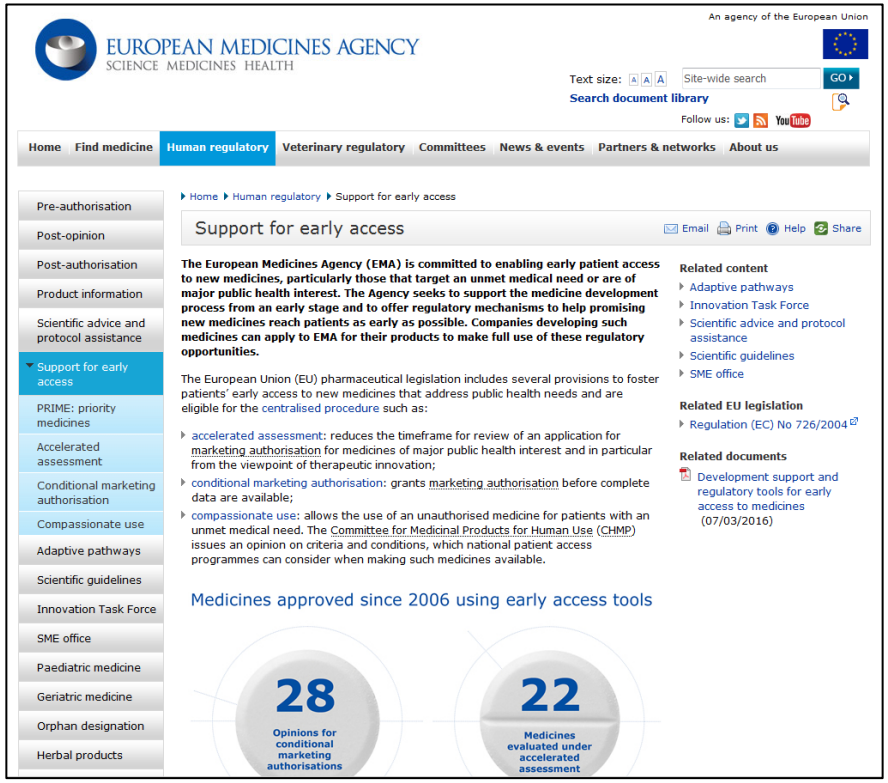
Revisions to CHMP Guideline on accelerated assessment

- Stressing the importance of proactive **early dialogue** to advise on MAA submission strategy
- More detailed guidance **how to justify** major public health interest based on the existing three key elements (existing methods, unmet medical need, and strength of evidence)
- Optimisation of the **evaluation phases** to reach a CHMP opinion within 150 days (now 90 + 30 + 30 days)*
- Acknowledgment that **comprehensive clinical data** may not be available in certain situations (e.g. accelerated assessment for conditional marketing authorisation applications)

* For ATMPs, timetable will be arranged to include review by the Committee for Advanced Therapies

One step towards EU network strategy to 2020 objectives

- Better overview of existing tools
- Encourage early dialogue
- Improved accelerated assessment procedure
- Prospective planning and optimisation of use of CMA
- Consolidation through PRIME for priority medicines



EUROPEAN MEDICINES AGENCY

Thank you for your attention

Further information

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**