EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Early dialogue

EMA- EuropaBio Information Day

Focus on PRIME

Presented by Rob Hemmings, MHRA, SAWP chair, CHMP
22-11-2016

Disclaimer

Early access tools: Overview

PRIME

Major public health interest, unmet medical need.

Dedicated and reinforced support.

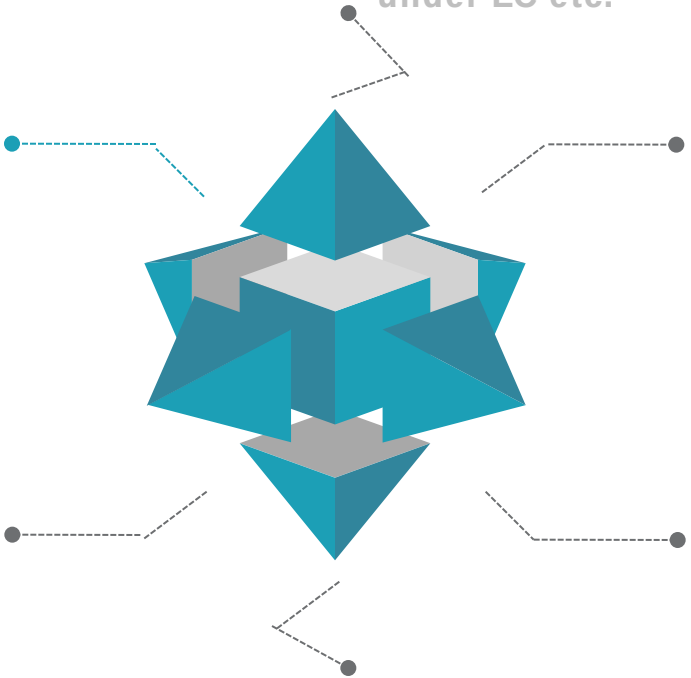
Enable accelerated assessment.

Better use of existing regulatory & procedural tools.

Accelerated Assessment

Major public health interest, unmet medical need.

Reduce assessment time to 150 days.



Early access tools: **Patients**

Other…Compassionate Use, MA under EC etc.

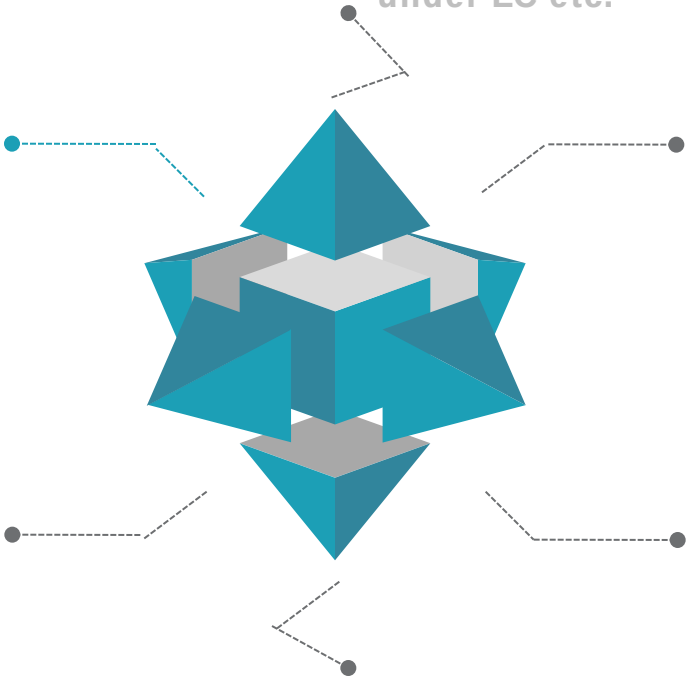
PRIME

Major public health interest, unmet medical need.

Dedicated and reinforced support.

Enable accelerated assessment.

Better use of existing regulatory & procedural tools.



Adaptive Pathways

Scientific concept of development and data generation.

Iterative development with use of real-life data.

Engagement with other healthcare-decision makers.

Accelerated Assessment

Major public health interest, unmet medical need.

Reduce assessment time to 150 days.

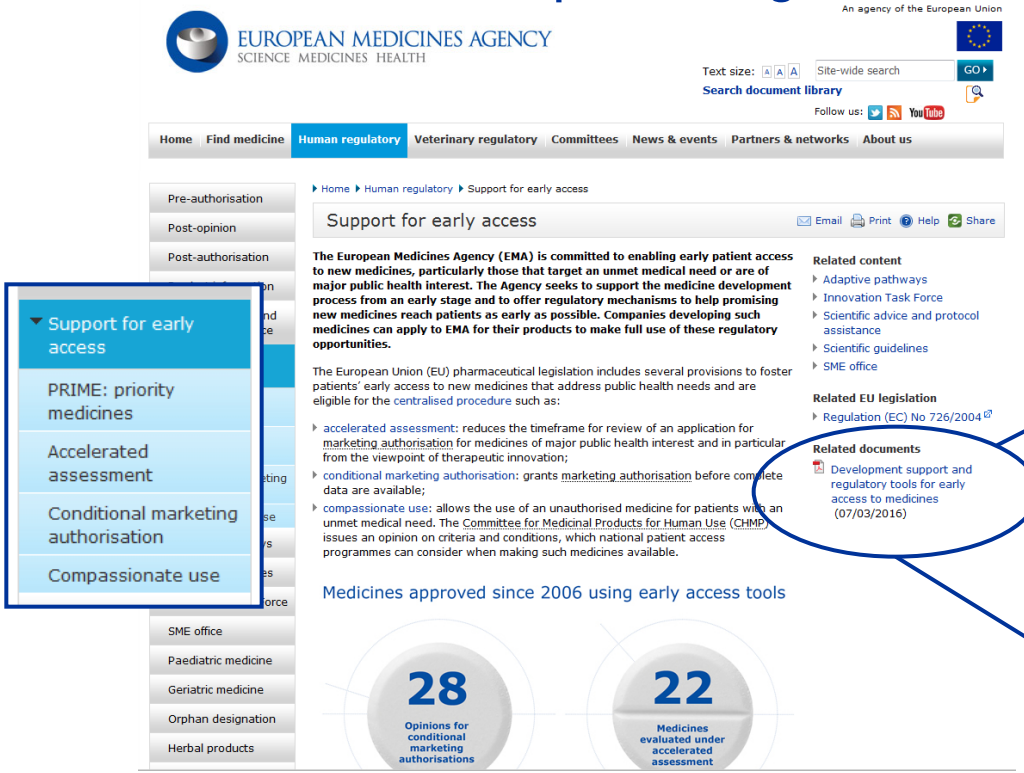
Conditional MA

Unmet medical need, seriously debilitating or life-threatening disease, a rare disease or use in emergency situations.

Early approval of a medicine on the basis of less complete clinical data.

Parallel advice

Launch of PRIME and updated guidelines




EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 March 2016
EMA/53101/2015
Human Medicines Research and Development Support Division

Development support and regulatory tools for early access to medicines

The EU pharmaceutical legislation includes a number of provisions in Regulation (EC) No 726/2004 aimed at fostering patients' early access to new medicines that address public health needs and are eligible to the **centralised procedure**, such as:

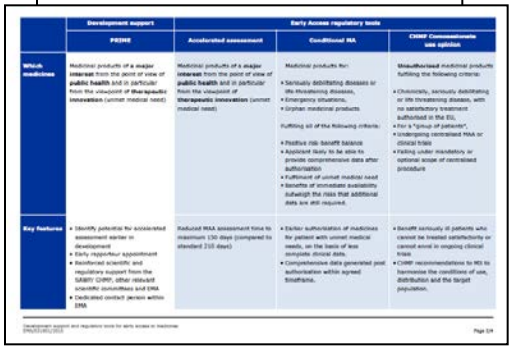
- **accelerated assessment** procedure which reduces the timeframe for review of an application for marketing authorisation from a maximum of 210 days to 150 days for medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation,
- for certain categories of medicinal products, the possibility to obtain **a conditional** marketing authorisation on the basis of less complete data than is normally the case and subject to specific obligations and additional comprehensive data to be provided post-authorisation. Conditional marketing authorisations are valid for one year on a renewable basis,
- the possibility for a **compassionate use opinion** by the CHMP defining at European level the criteria and conditions for use of medicinal products which are made available to patients through national patients' access programmes (prior to a marketing authorisation).

To optimise the use of the above regulatory tools, EMA has launched the **PRIME** scheme to support development of medicinal products of major public health interest through early and enhanced scientific and regulatory dialogue. This tool targets support to certain type of products eligible for accelerated assessment and falling within the scope of the centralised procedure. It builds also on existing regulatory tools in place within the European Union (EU) legal framework, including scientific advice/protocol assistance.

The table overleaf provides a high-level overview of the above legislative and development support tools to help sponsors identify when and how to use them.

However, there are a number of other development support activities, not covered in this tabular overview, carried out by the Agency including the following:

- The Innovation Task Force (ITF) which is a multidisciplinary group providing a forum for informal early dialogue with applicants, in particular micro, small and medium enterprises (SMEs) and academic sponsors, to proactively identify scientific, technical and regulatory issues related to emerging therapies and technologies.



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

PRIME scheme - Goal & Scope

To foster the development of ***medicines with major public health interest.***

Reinforce scientific and regulatory advice

- Foster and facilitate early interaction
- Raise awareness of requirements earlier in development

Optimise development for robust data generation

- Focus efficient development
- Promote generation of robust and high quality data

Enable accelerated assessment

- Facilitated by knowledge gained throughout development
- Feedback of relevant SA aspects to CHMP

Building on existing framework;

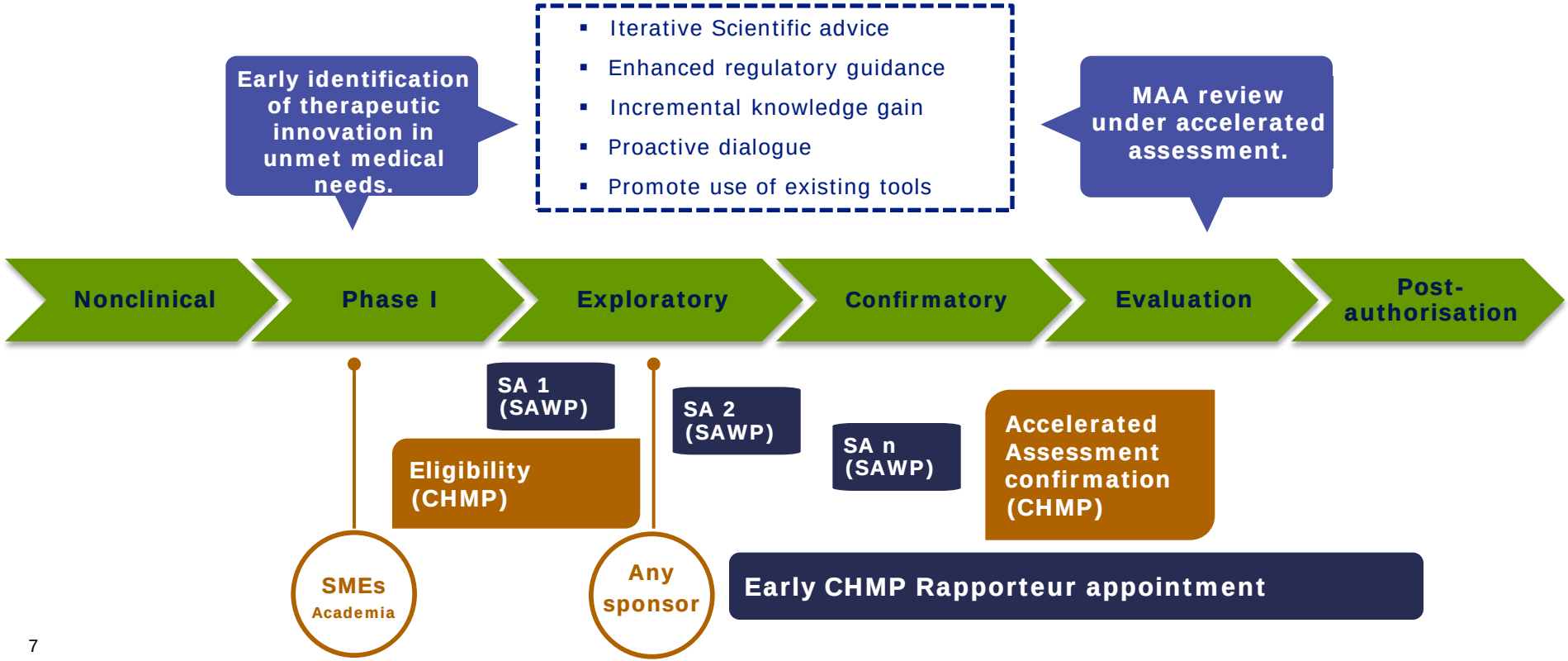
Eligibility according to existing ‘Accelerated Assessment criteria’

Features of the PRIME scheme

Early access tool, supporting patient access to innovative medicines.

- **Written confirmation of PRIME eligibility** and potential for accelerated assessment;
- **Early CHMP Rapporteur appointment** during development;
- **Kick off meeting** with multidisciplinary expertise from EU network;
- **Enhanced scientific advice** at key development milestones/decision points;
- **EMA dedicated contact point**;
- **Fee incentives** for SMEs and academics on Scientific Advice requests.

Overview of PRIME scheme



Justification for eligibility to PRIME

For products under development yet to be placed on the EU market

Unmet medical need

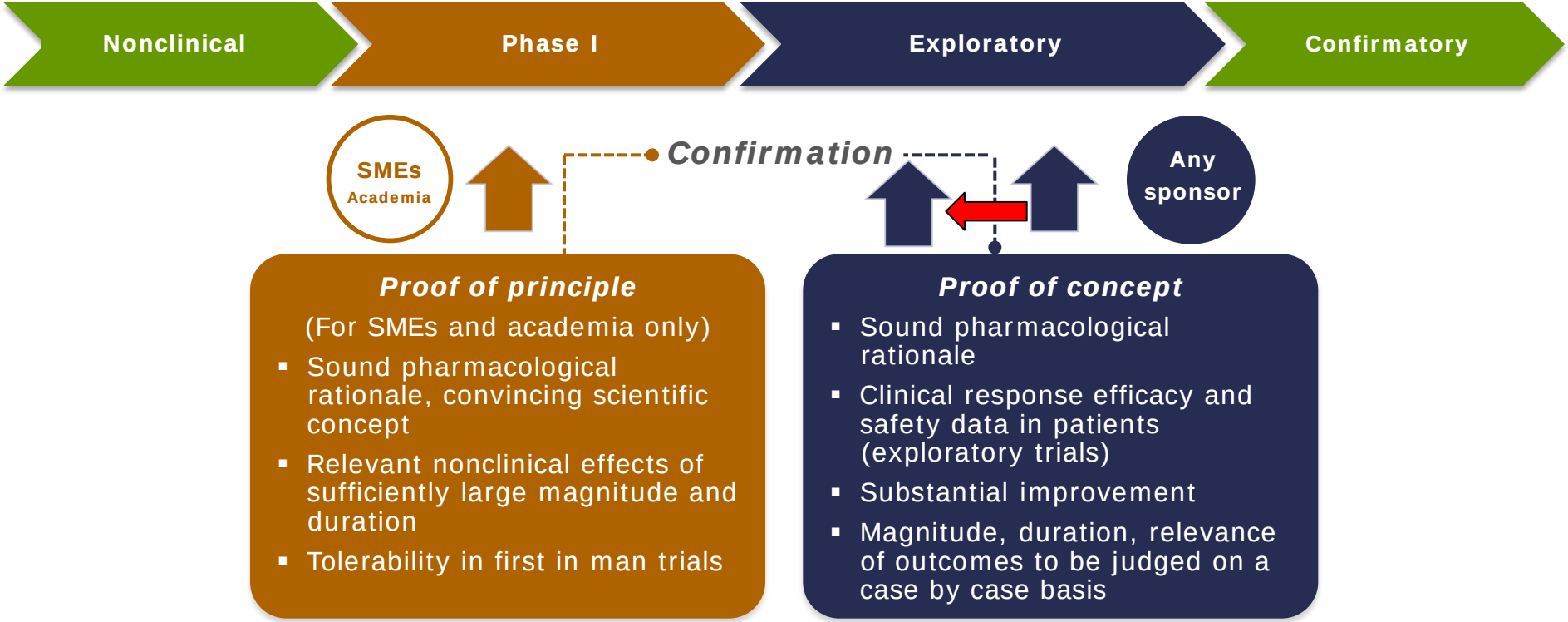
- Epidemiological data about the disease
- Description of available diagnostic, prevention and treatment options/standard of care (SOC), their effect and how medical need is not fulfilled

Potential to significantly address the unmet medical need

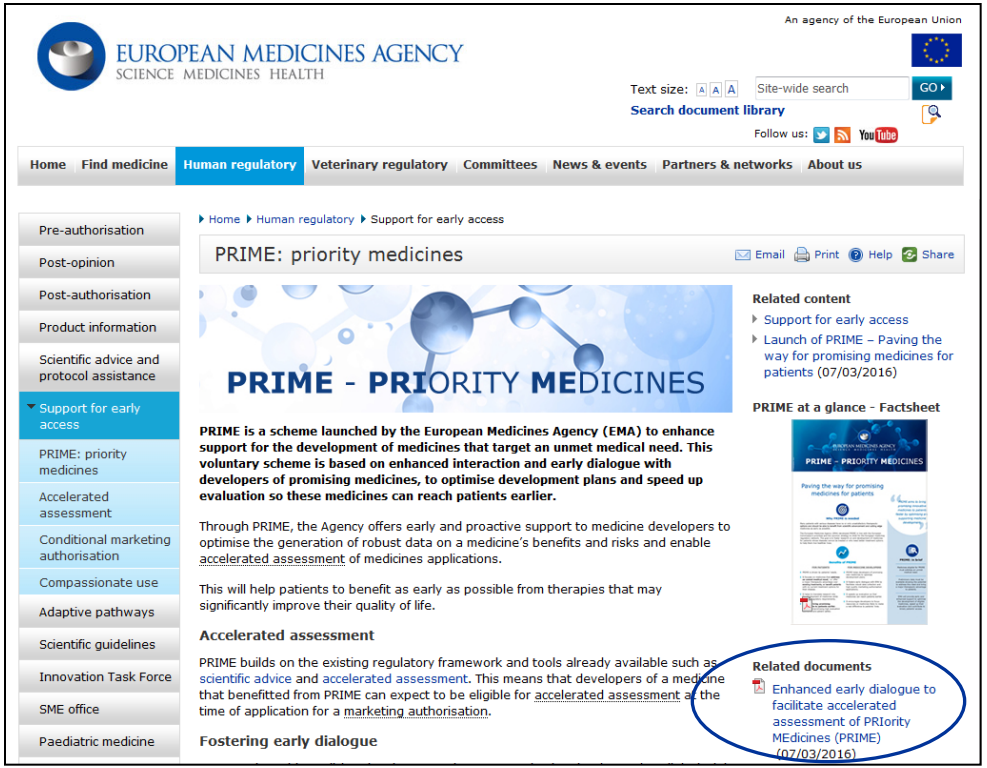
- Description of observed and predicted effects, clinical relevance, added value and impact
- If applicable, expected improvement over existing treatments

Data required at different stages of development

Entry points PRIME eligibility and required evidence



PRIME webpage and supporting documents



Factsheet in lay language

Q&A, templates, application form for applicants

prime@ema.europa.eu

PRIME eligibility requests received 7 March – 21 September 2016

EUROPEAN MEDICINES AGENCY

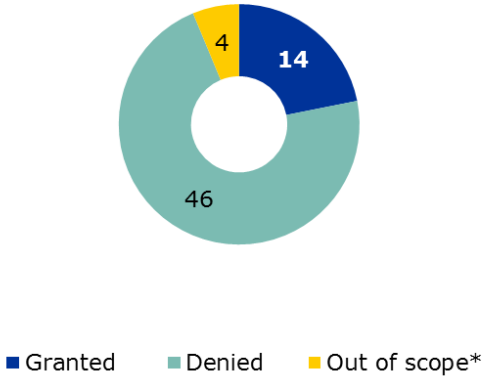
6 cycles

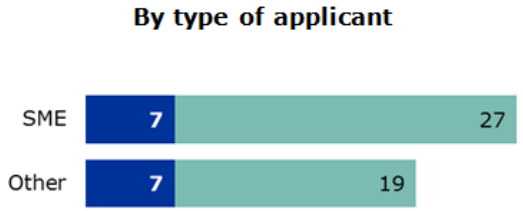
60+ eligibility requests

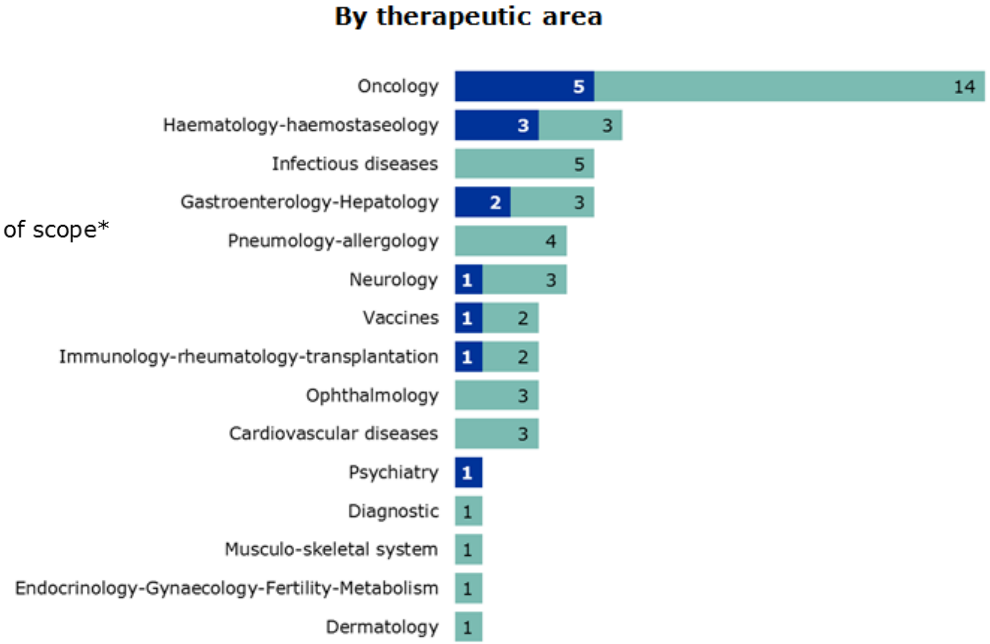
14 granted

- 50% SME

- 50% ATMP







Early observations and experiences: eligibility

- Challenge to quantify and to contrast unmet medical need
- Potential to significantly address the unmet medical need: pharmacological insights vs clinical data
- Other issues:
  - Stage of development
  - Competitor development
  - Identified or potential safety issues

Early observations and experiences

- Limited interest to date in ‘POP’ entry?
- Not dominated by large pharma
- Will Onc and Haem continue to dominate?
  - Is it inevitable?
  - Is eligibility ‘easier’ for some indications: stratified population, observable responses, rapid onset?

Early observations and experiences

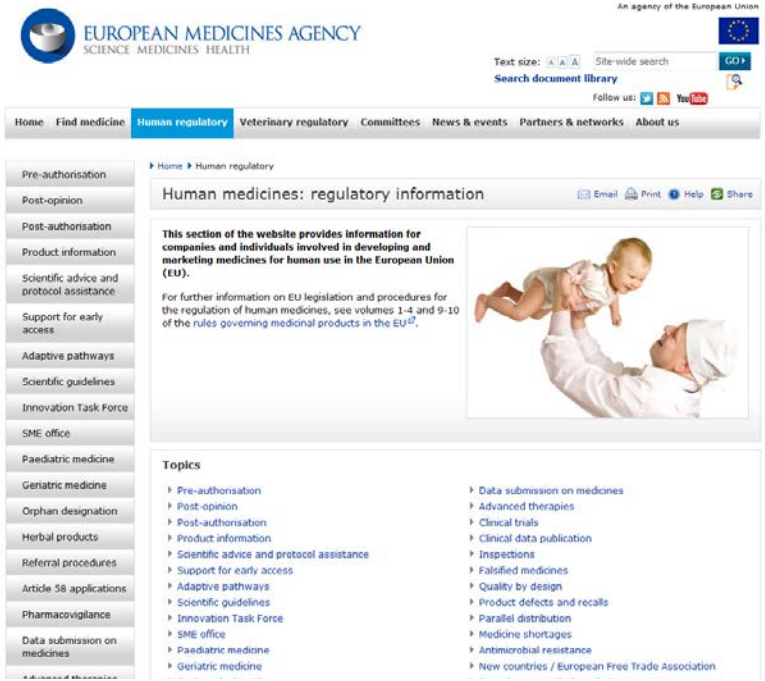
- Strong engagement from the network
  - Oversight group
  - Kick-off meetings

- Kick-off meetings
  - ‘Sit-rep’
  - Schedule for regulatory interactions
  - Communication with Rapporteurs
  - Opportunities foe early submission

Future … some personal thoughts

- Formal review will be required
  - Increased transparency without compromising confidentiality?
  - Clarity on other considerations around eligibility
- Can a PRIME designation be useful for other stakeholders?
- Interactions on the third axis: Company ↔ Rapporteur

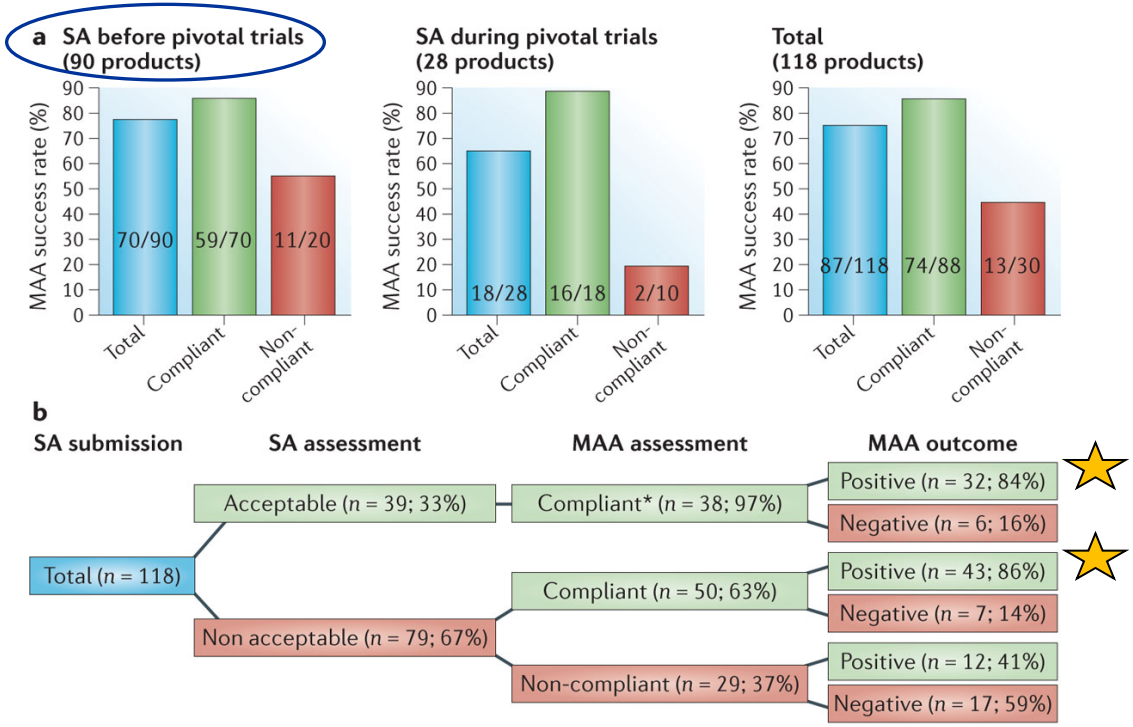
If PRIME is not the right tool



EMA still can provide support through…

- EU innovation network
- Innovation Task Force
- Scientific Advice
- SME office
- ATMP certification
- Paediatric early interaction meetings
- Accelerated Assessment
- Pre-submission meetings

Scientific advice



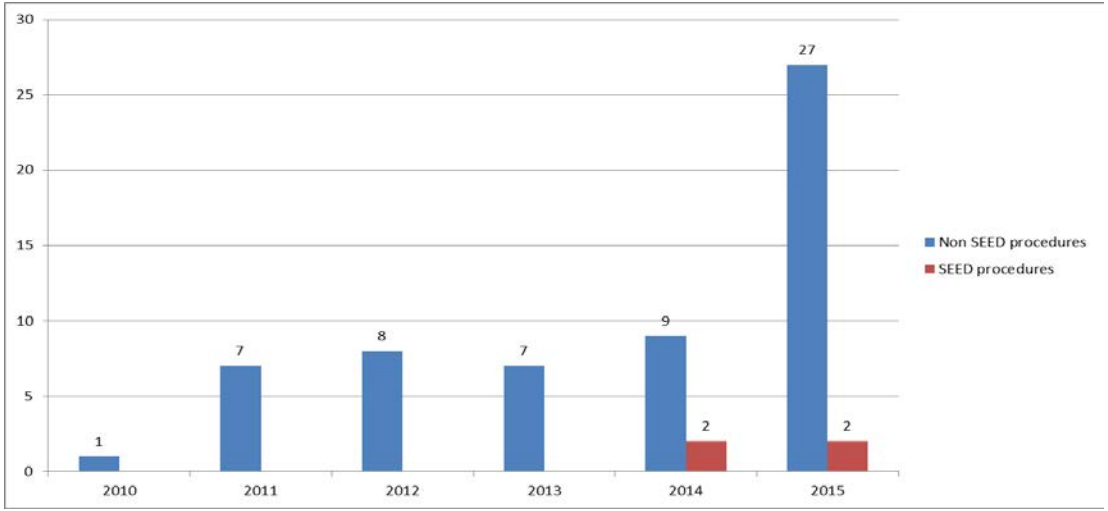
Nature Reviews | Drug Discovery

- Sponsors prefer early interactions
- Earlier SA is associated with higher MAA success rate
- Compliance with SA recommendations on clinical trial design associated with
  - Higher MAA success rate
  - Less major objections
  - Shorter MAA procedure

Hofer M.P., Jakobsson C., Zafiropoulos N., Vamvakas S., Vetter T., Regnstrom J., Hemmings R.J., Regulatory watch: Impact of scientific advice from the European Medicines Agency, Nature Reviews Drug Discovery, Vol 14(5), pp. 302-303.

Parallel EMA/HTA scientific advice

Completed parallel advice procedures / year



Can parallel advice help?

- Collect the right evidence for each stakeholder
- One trial / development plan
- Various players- round table discussion
- Find solutions for efficient data collection
- Lifecycle approach

Report and guidance published

•Collated information on participating HTAs

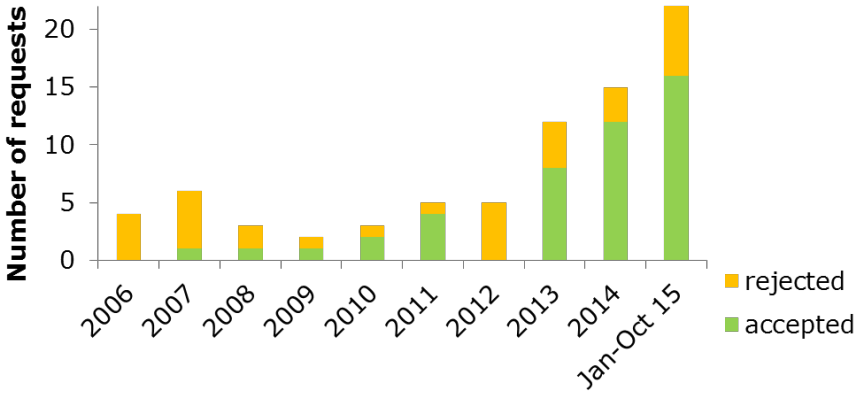
•Shaping evidence development

•Companies to engage and plan

•Important platform

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/03/news_detail_002499.jsp&mid=WC0b01ac058004d5c1

Accelerated assessment



Robust decision making under accelerated timelines requires a mature submission, which should be subject to pre-filing discussions.

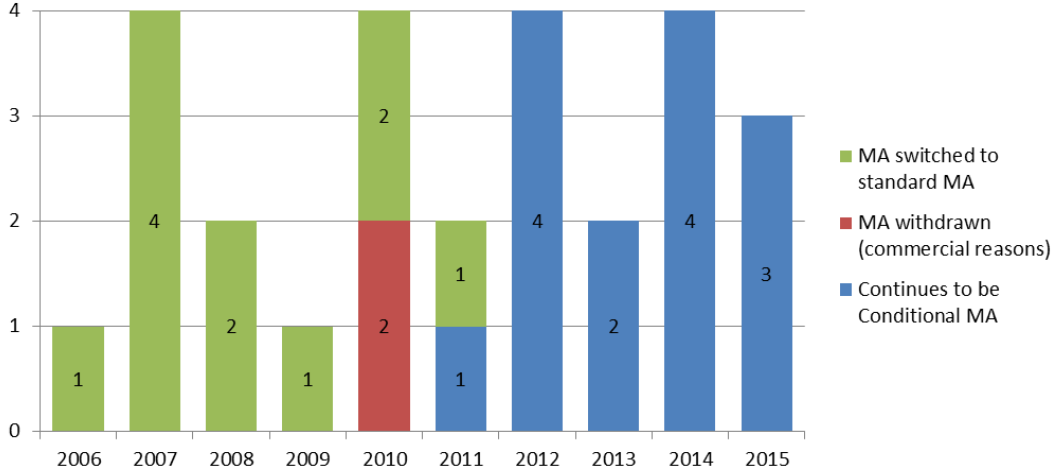
Only half of these MAA are completed under accelerated timelines

Reasons for reverting to standard timelines during the MAA evaluation:

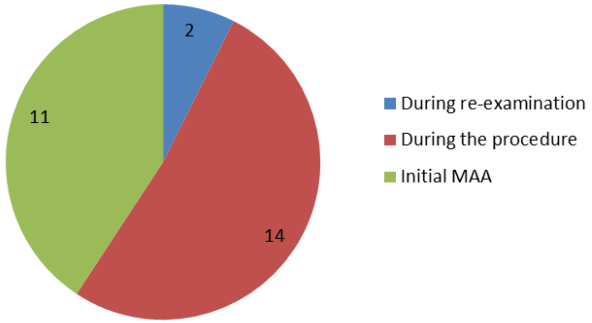
- Critical GCP issues identified in inspections
- Major objection on adequacy of extrapolation
- Need for a GMP inspection
- Major clinical objection questioning the clinical relevance of the effects
- Numerous major objections including need for re-analysis of efficacy data
- Significant quality major objection

Conditional Marketing Authorisation

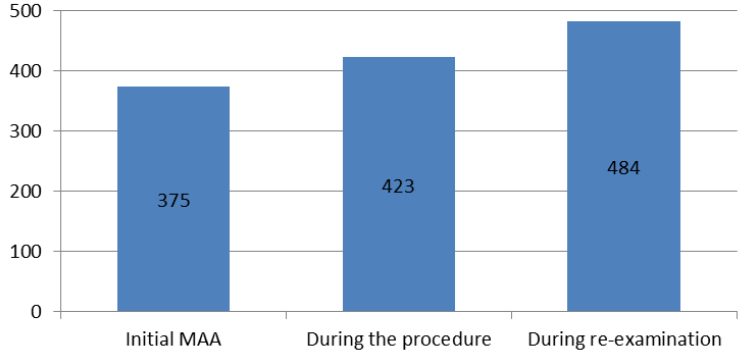
Overview of Conditional marketing authorisations by year of granting and current status



CMAs by stage of procedure when CMA was first considered



Average duration of procedure (including clock-stops) by stage of procedure when CMA was first considered



Importance of early dialogue and prospective planning

Thanks for your attention

Acknowledgements to multiple EMA colleagues, in particular Jordi and Zahra.