



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



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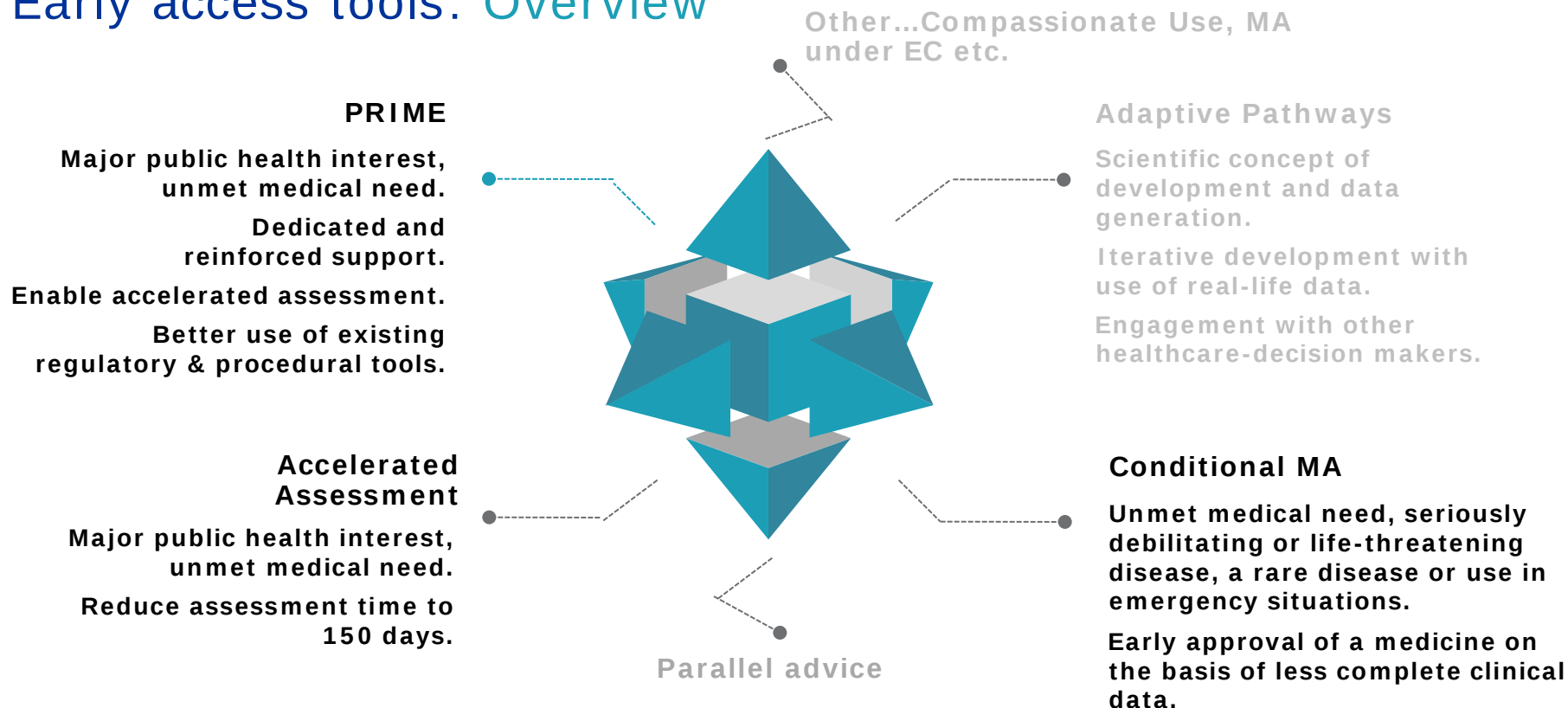


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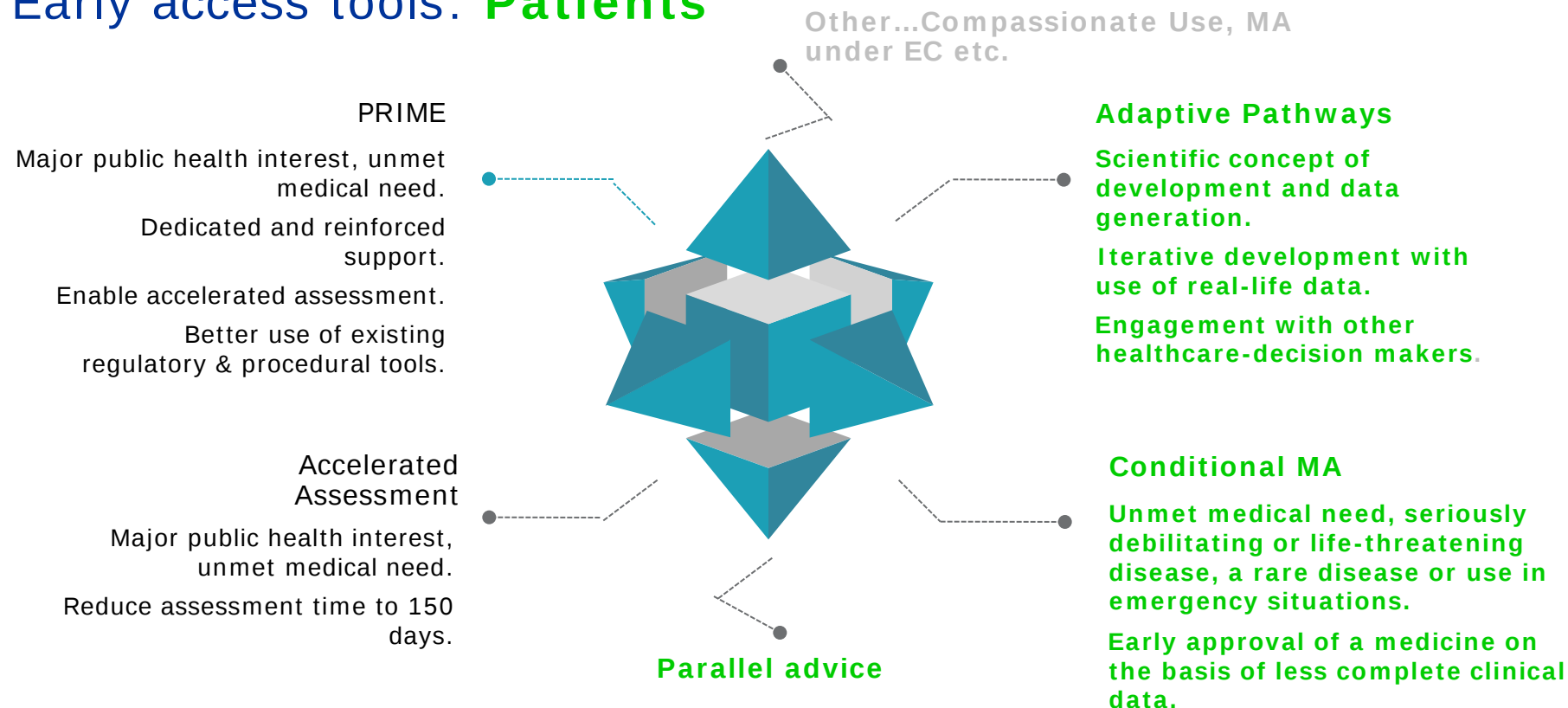


Early access tools: Overview





Early access tools: **Patients**



Launch of PRIME and updated guidelines



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Pre-authorisation
Post-opinion
Post-authorisation

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Support for early access

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The European Medicines Agency (EMA) is committed to enabling early patient access to new medicines, particularly those that target an unmet medical need or are of major public health interest. The Agency seeks to support the medicine development process from an early stage and to offer regulatory mechanisms to help promising new medicines reach patients as early as possible. Companies developing such medicines can apply to EMA for their products to make full use of these regulatory opportunities.

The European Union (EU) pharmaceutical legislation includes several provisions to foster patients' early access to new medicines that address public health needs and are eligible for the centralised procedure such as:

- accelerated assessment: reduces the timeframe for review of an application for marketing authorisation for medicines of major public health interest and in particular from the viewpoint of therapeutic innovation;
- conditional marketing authorisation: grants marketing authorisation before complete data are available;
- compassionate use: allows the use of an unauthorised medicine for patients with an unmet medical need. The Committee for Medicinal Products for Human Use (CHMP) issues an opinion on criteria and conditions, which national patient access programmes can consider when making such medicines available.

Related content

- Adaptive pathways
- Innovation Task Force
- Scientific advice and protocol assistance
- Scientific guidelines
- SME office

Related EU legislation

- Regulation (EC) No 726/2004

Related documents

- Development support and regulatory tools for early access to medicines (07/03/2016)

Medicines approved since 2006 using early access tools

28

Opinions for conditional marketing authorisations

22

Medicines evaluated under accelerated assessment

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA/31801/2015
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 types 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 overview 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 table.

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.

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	Development support	Accelerated assessment	Conditional MA	CHMP Compassionate use opinion
Which medicines	Medicinal products of a major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation (current medicine need)	Medicinal products of a major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation (current medicine need)	Medicinal products for: • Seriously debilitating diseases or life threatening conditions; • Emergency situations; • Orphan medicinal products; • Putting all of the following criteria: • Positive risk/benefit balance; • Applicant ready to be able to provide comprehensive data after authorisation; • Fulfilment of unmet medical need; • Benefit of immediate availability outweighs the risks that additional data are not required.	Unauthorised medicinal products falling the following criteria: • Characteristic, seriously debilitating or life threatening diseases, with no satisfactory treatment authorised in the EU; • For a "signal of patient"; • Undergoing accelerated MA or clinical trial; • Filling under mandatory or national scope of restricted products
Key features	• Identify potential for accelerated assessment prior to development • Early regulatory engagement • Enhanced scientific and regulatory support from the CHMP, CHMP other research member committees and EMA • Tailored medical advice within EMA	Reduced MA assessment time to maximum 150 days (compared to standard 210 days)	• Earlier authorisation of medicines by joint with national medical needs, on the basis of less complete clinical data; • Comprehensive data generated post-authorisation will be agreed	• Benefit seriously ill patients who cannot be treated adequately or cannot access to ongoing clinical trials; • CHMP recommendations to MS to harmonise the conditions of use, distribution and the target population



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

Early identification
of therapeutic
innovation in
unmet medical
needs.

- Iterative Scientific advice
- Enhanced regulatory guidance
- Incremental knowledge gain
- Proactive dialogue
- Promote use of existing tools

MAA review
under accelerated
assessment.

Nonclinical

Phase I

Exploratory

Confirmatory

Evaluation

Post-
authorisation

SA 1
(SAWP)

Eligibility
(CHMP)

SA 2
(SAWP)

SA n
(SAWP)

Accelerated
Assessment
confirmation
(CHMP)

SMEs
Academia

Any
sponsor

Early CHMP Rapporteur appointment

Justification for eligibility to PRIME

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



Unmet medical need

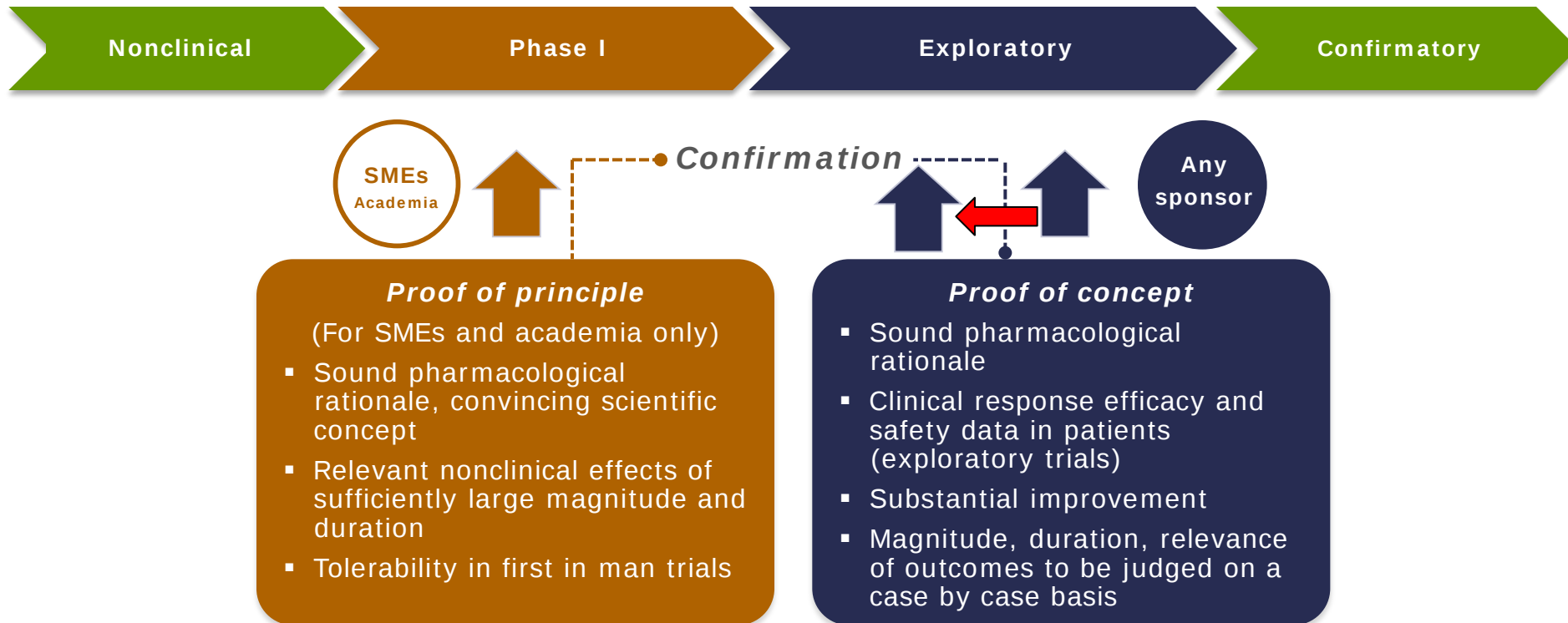
- Epidemiological data about the disease
- Description of available diagnostic, prevention and treatment options/standard of care (SOC), their effect and how medical need is not fulfilled

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

The screenshot shows the EMA website with the 'Human regulatory' tab selected. The main content area is titled 'PRIME: priority medicines'. It includes a sidebar with navigation links like 'Pre-authorisation', 'Post-opinion', and 'Support for early access'. The main text describes PRIME as a scheme to enhance support for the development of medicines that target an unmet medical need. It mentions that PRIME builds on existing regulatory frameworks and tools. A 'Related documents' section is circled in blue, containing a link to 'Enhanced early dialogue to facilitate accelerated assessment of Priority Medicines (PRIME) (07/03/2016)'.

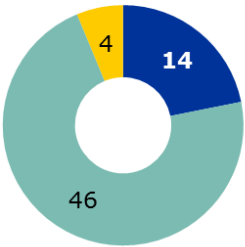
This is a factsheet titled 'PRIME - PRIORITY MEDICINES' with the subtitle 'Paving the way for promising medicines for patients'. It explains the purpose of PRIME, which is to bring promising innovative medicines to patients faster by optimising and supporting medicine development. It lists benefits for patients, such as faster access to new medicines, and for medicine developers, such as enhanced early dialogue and accelerated assessment. It also mentions that PRIME is a scheme launched by the EMA to enhance support for the development of medicines that target an unmet medical need.

Factsheet in lay language

This document is titled 'European Medicines Agency Guidance for applicants seeking access to PRIME scheme'. It provides guidance on how to apply for PRIME. It states that the guidance is intended to help applicants understand the PRIME scheme and how to apply. It also mentions that the guidance is updated regularly to reflect new developments in the scheme. The document is dated 1 March 2016 and is available in English, French, and German.

Q&A, templates, application form for applicants

6 cycles
60+ eligibility
requests
14 granted
- 50 % SME
- 50 % ATMP

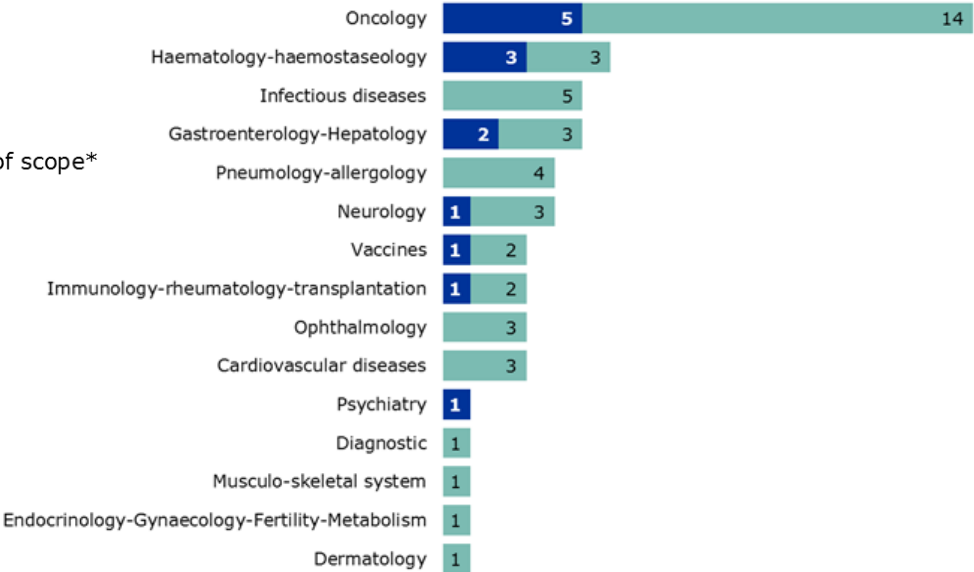


■ Granted ■ Denied ■ Out of scope*

By type of applicant



By therapeutic area



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 for 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

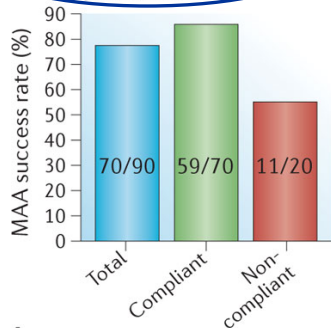


EMA still can
provide support
through...

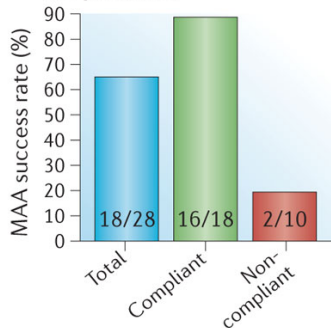


Scientific advice

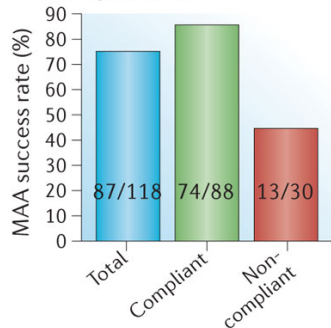
a SA before pivotal trials (90 products)



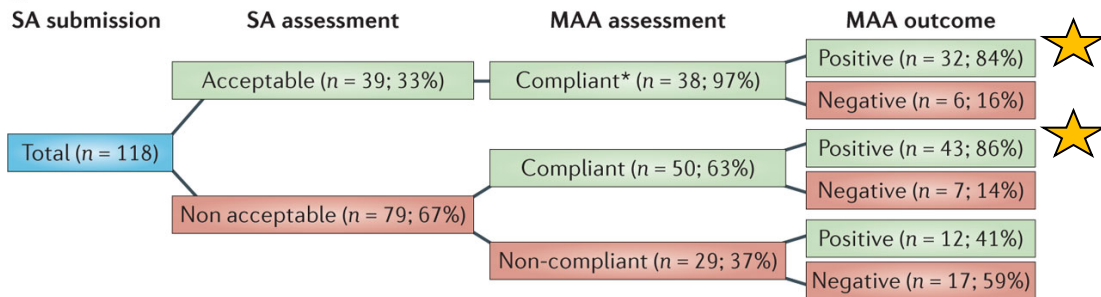
SA during pivotal trials (28 products)



Total (118 products)



b

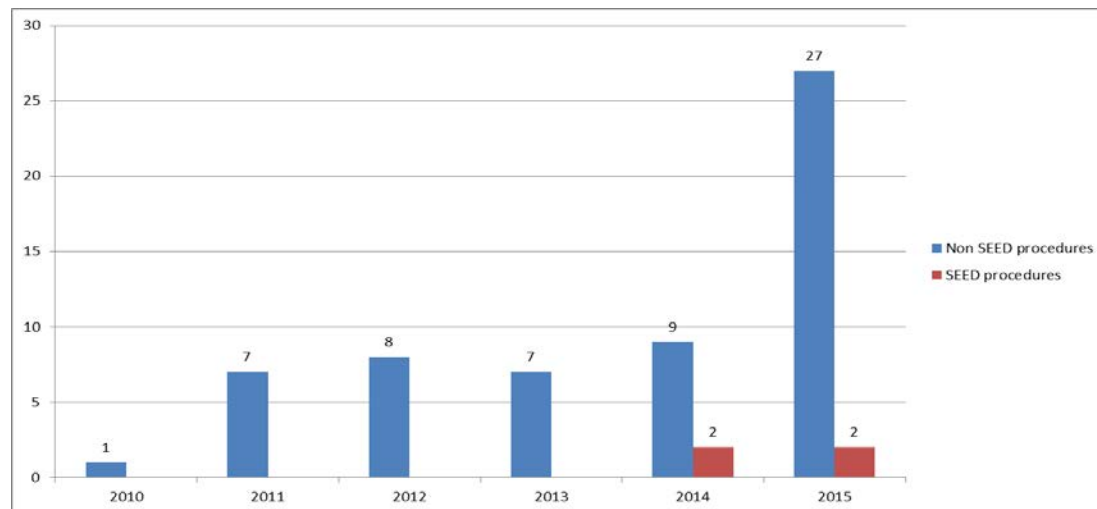


- Sponsors prefer early interactions
- Earlier SA is associated with higher MAA success rate
- Compliance with SA recommendations on clinical trial design associated with
 - Higher MAA success rate
 - Less major objections
 - Shorter MAA procedure



Parallel EMA/HTA scientific advice

Completed parallel advice procedures / year



Can parallel advice help?

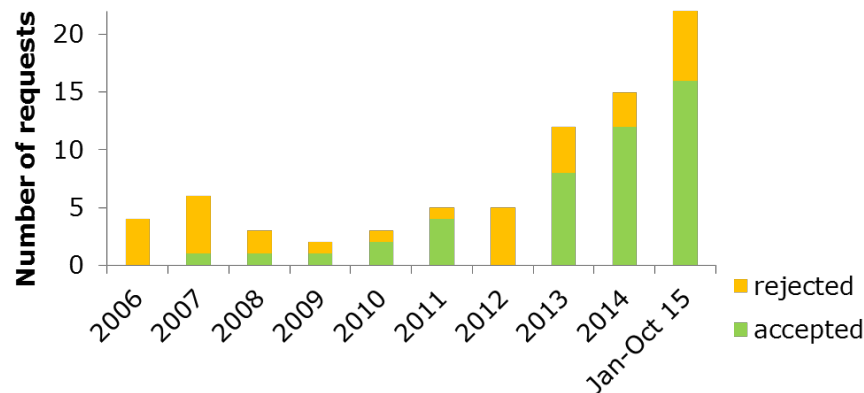
- Collect the right evidence for each stakeholder
- One trial / development plan
- Various players- round table discussion
- Find solutions for efficient data collection
- Lifecycle approach

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

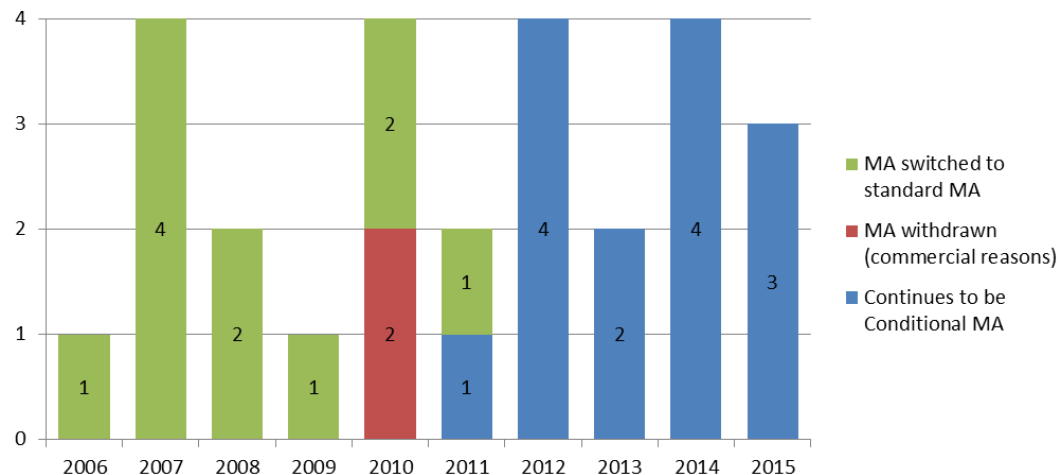
Reasons for reverting to standard timelines during the MAA evaluation:

- 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



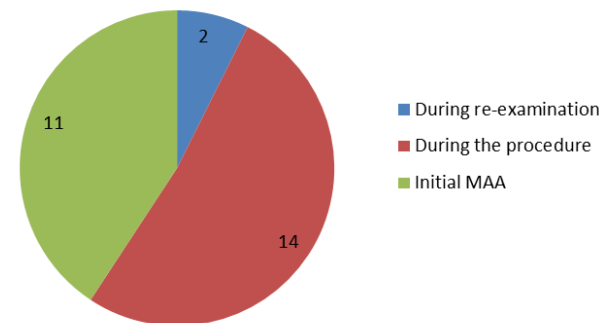
Conditional Marketing Authorisation

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

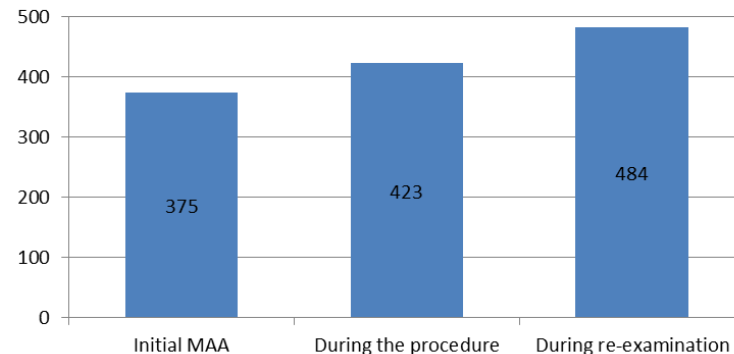


Importance of early dialogue and prospective planning

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





Thanks for your attention

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