# Protocol Assistance/PRIME/parallel consultation

Workshop on Support for Orphan Medicines Development

Presented by Armando Magrelli on 30 November 2020
Vice-chair | Committee for Orphan Medicinal Products (COMP) | EMA

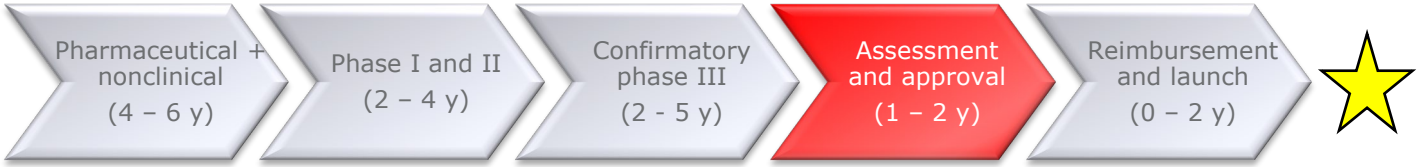
# Disclaimer



The presenter does not have any conflict of interests.

# The typical long route of medicines to patients

Development phase:



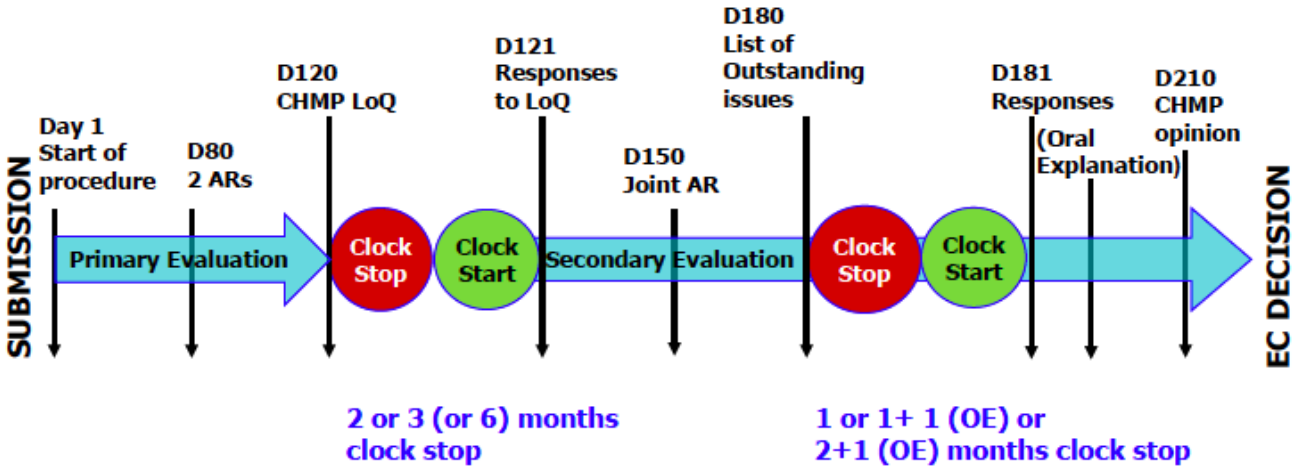

- Chance of reaching access for a product entering the development phase:

0.01-0.1% 5-10% 50-60% 75-90%

Regulatory provisions primarily targeting the time to access:
•Conditional MA (CMA),
•Accelerated Assessment (AA),
•Compassionate Use (CU)…

Regulatory provisions primarily targeting the risk of development failure:
•Scientific advice
•Support to SMEs …

# Standard timetable until marketing authorisation in centralised procedure




**D120 LoQs**: major objections (MOs) or other concerns (OCs)

**OE**: presentation by Company – questions – discussion within committee – (trend) vote

# Early access tools: Overview

**PRIME**

**Major public health interest, unmet medical need.**

**Dedicated and reinforced support.**

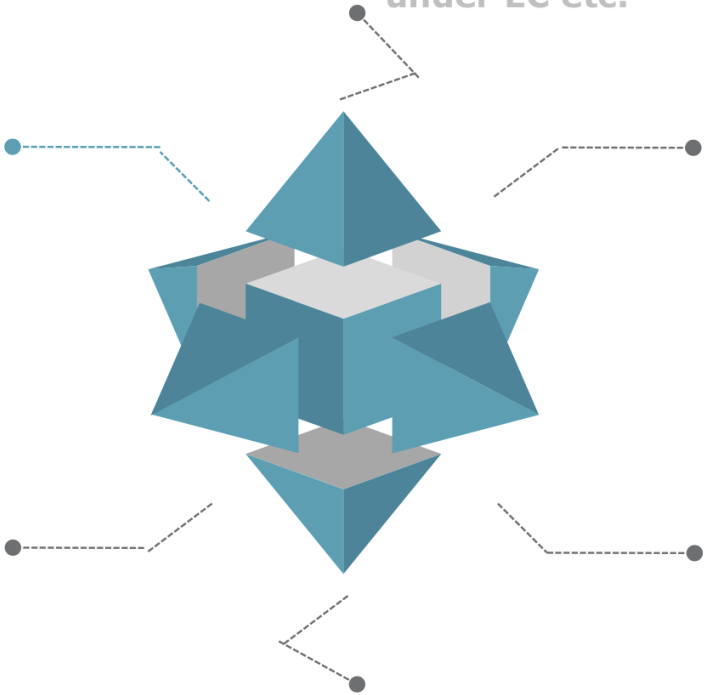
**Enable accelerated assessment.**

**Better use of existing regulatory & procedural tools.**

**Accelerated Assessment**

**Major public health interest, unmet medical need.**

**Reduce assessment time to 150 days.**



Other…Compassionate Use, MA under EC etc.

**Adaptive Pathways**

**Scientific concept of development and data generation.**

**Iterative development with use of real-life data.**

**Engagement with other healthcare-decision makers.**

**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

# Early access tools: **Patients**

Other…Compassionate Use, MA under EC etc.

## PRIME

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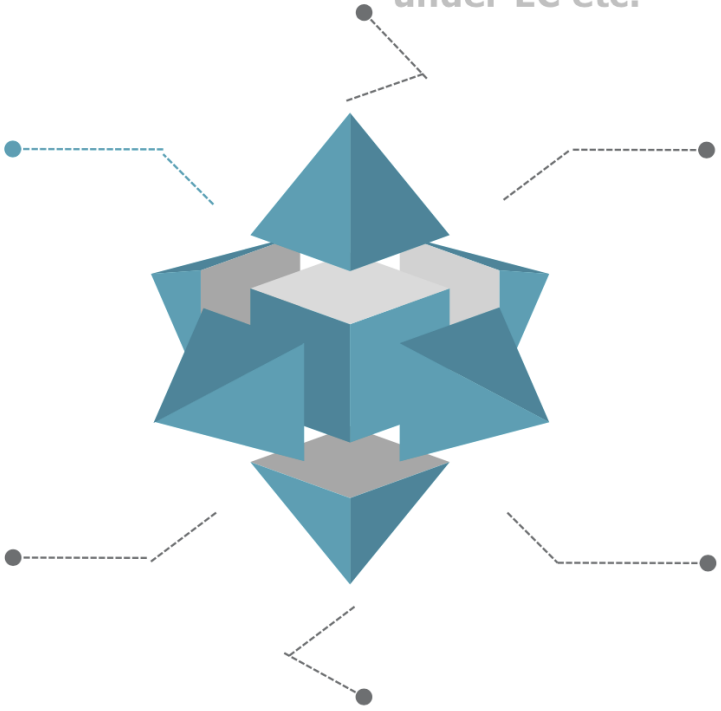

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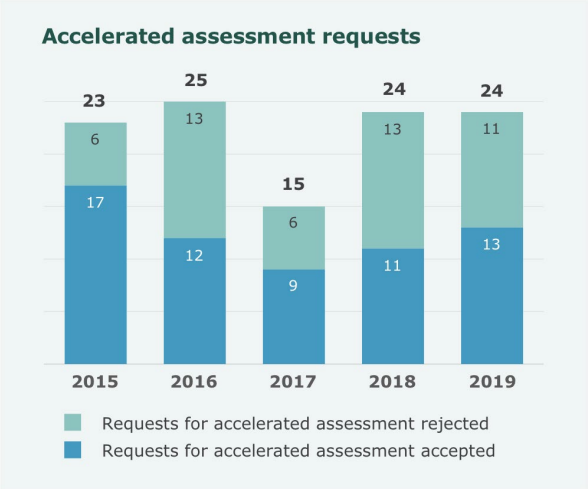
# Accelerated assessment




***Only half of these MAA are completed under accelerated timelines***

<u>Reasons for reverting to standard timelines during the MAA evaluation:</u>

- 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

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

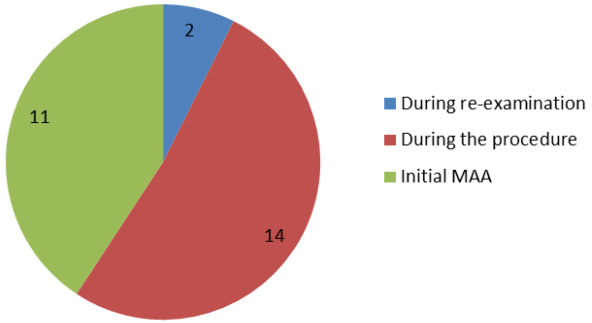
# Conditional Marketing Authorisation

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

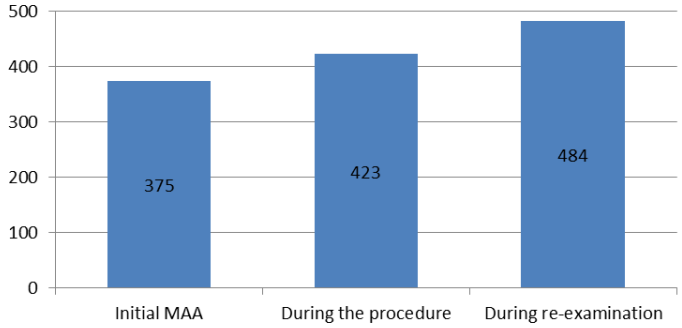
| CMA and switch to standard marketing authorisation (excluding withdrawals) | | | | | |
|---|---|---|---|---|---|
| | 2015 | 2016 | 2017 | 2018 | 2019 |
| Positive opinions for CMAs | 3 | 8 | 3 | 1 | 8 |
| Opinions recommending switch of CMA to standard marketing authorisation | 2 | 2 | 5 | 2[6] | 1 |

**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**




**Analysis 2006-2015**

# Scientific Advice and Protocol assistance

## General principles

• For human medicines, SA and protocol assistance are given by the Committee for Medicinal Products for Human Use (CHMP) on the recommendation of the Scientific Advice Working Party (SAWP).

• Prospective in nature- focusing on development strategies rather than pre-evaluation of data to support a MAA.

# The Scientific Advice procedure

**A streamlined 70-day procedure (maximum) with possibility of finalisation in 40 days. Several opportunities for interactions. SA can be given on any scientific question**

– Quality, non-clinical and clinical or Broad advice

– In parallel with the FDA (WHO)

– In parallel with HTAs/payers/patient organisations/academics

– Advice and Opinion on Qualification of novel methodologies/biomarkers

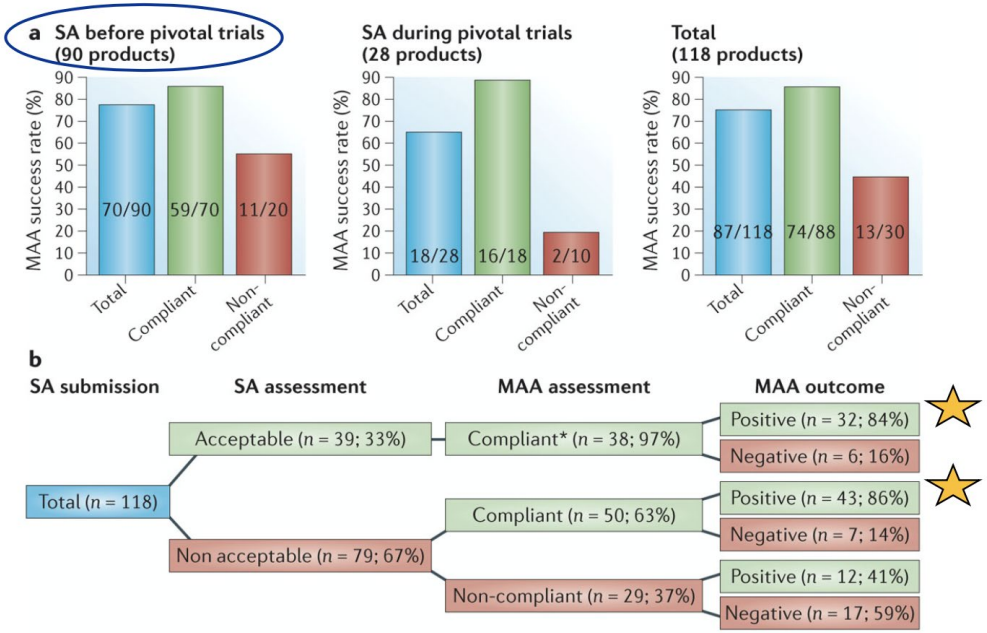
– Regulatory issues can be addressed a Pre-submission meetings SA can be requested at any time point of development

– Post-marketing advice is also available

– Paediatric SA during PIP procedure (with PDCO agreement)

– Allow sufficient time to address modifications Not legally binding but scientifically applicable throughout the EU

# Scientific advice



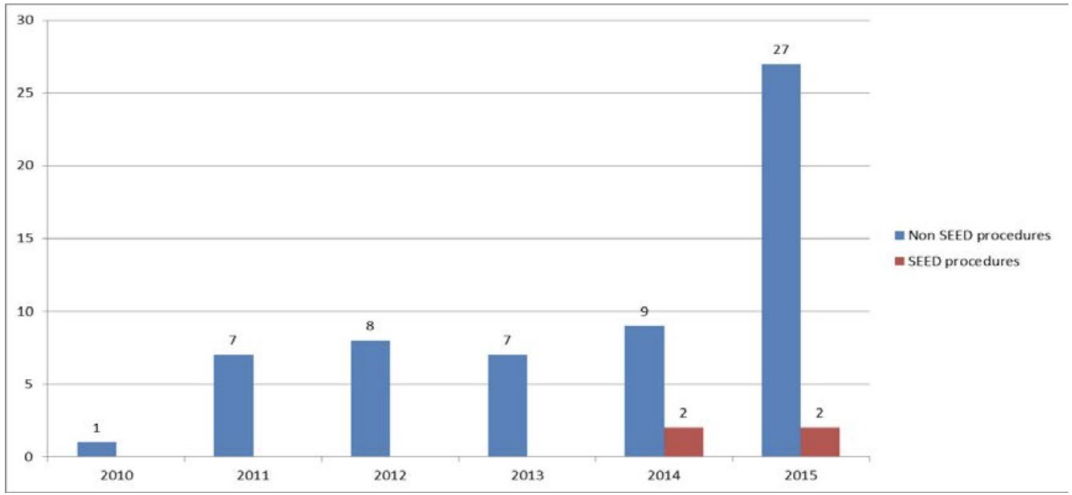

Nature Reviews | Drug Discovery

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.

- 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**




**Report and guidance published**

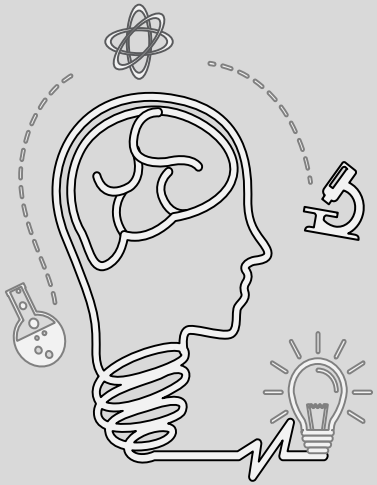
- Collated information on participating HTAs
- Shaping evidence development
- Companies to engage and plan
- Important platform

## Can parallel advice help?

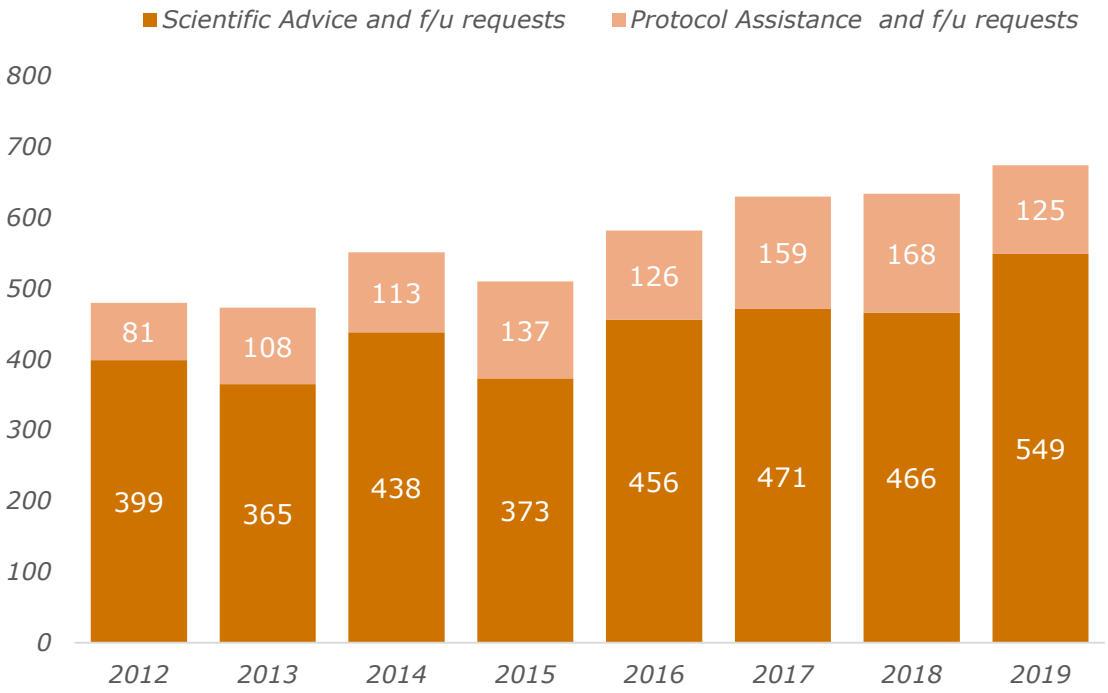
- Collect the right evidence for each stakeholder
- One trial / development plan
- Various players- round table discussion
- Find solutions for efficient data collection
- Lifecycle approach

https://www.ema.europa.eu/en/documents/report/report-pilot-parallel-regulatory-health-technology-assessment-scientific-advice_en.pdf

# Scientific Advice and Protocol Assistance



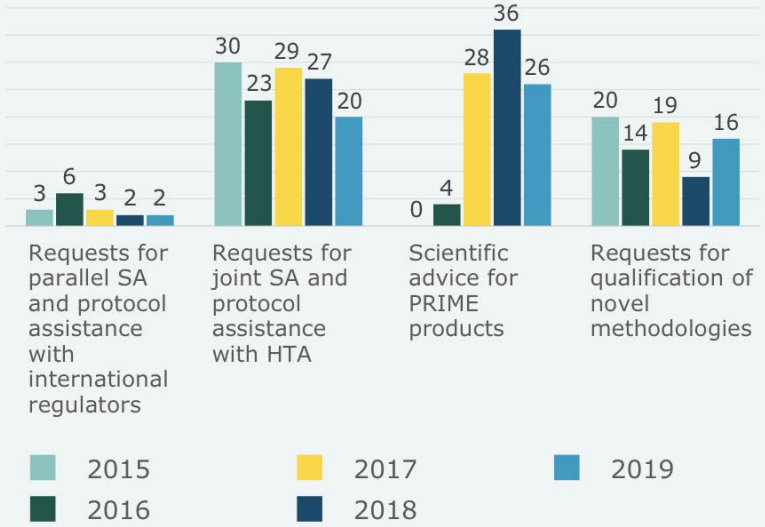
## Human medicinal Products



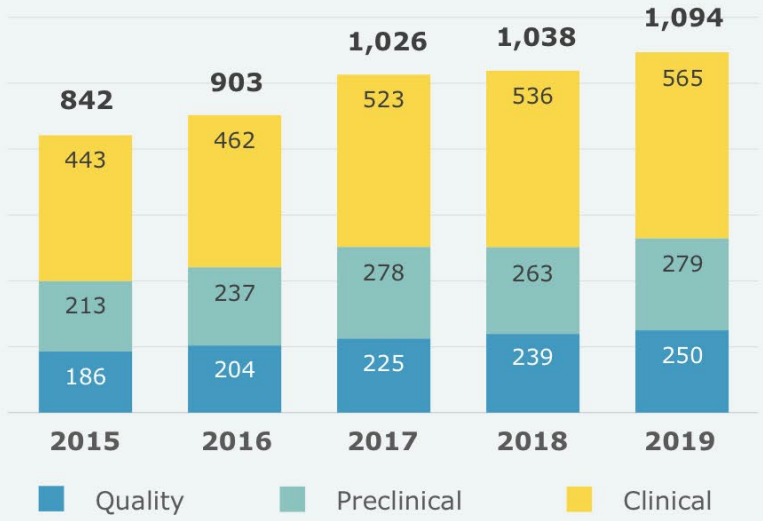

***11 qualification of novel methodologies out of 16 from SMEs***

# Scientific Advice and Protocol Assistance 2015-2019

## Scientific advice and protocol-assistance requests received - special programmes




## Scientific advice requests by topic




Many patients with serious diseases have no or only unsatisfactory therapeutic options and should be able to benefit from scientific advancement and cutting edge medicines as early as possible.

*PRIME aims to bring promising innovative medicines to patients faster by optimising and supporting medicine development*

# 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

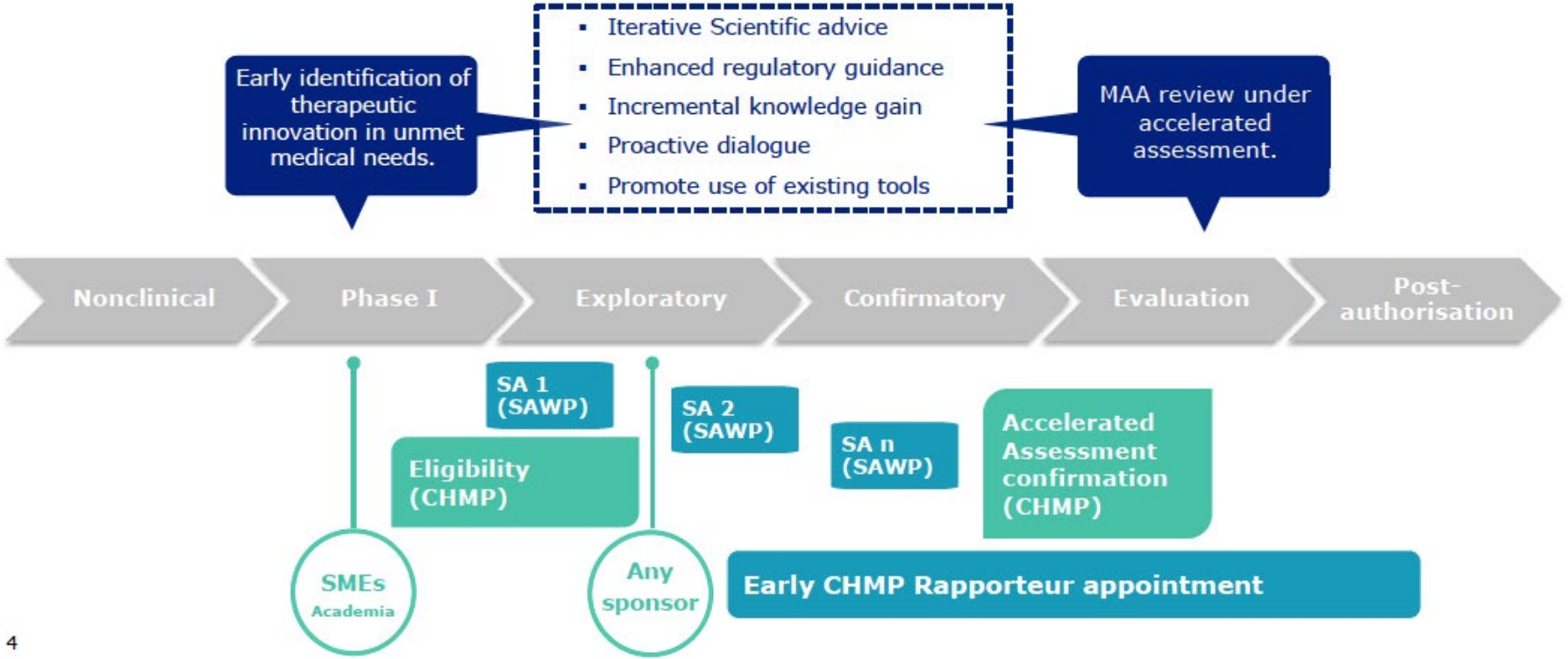
## Enable accelerated assessment

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

Building on existing framework;

Eligibility according to existing 'Accelerated Assessment criteria'

# Overview of PRIME scheme

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# 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, their effect and how medical need is not fulfilled

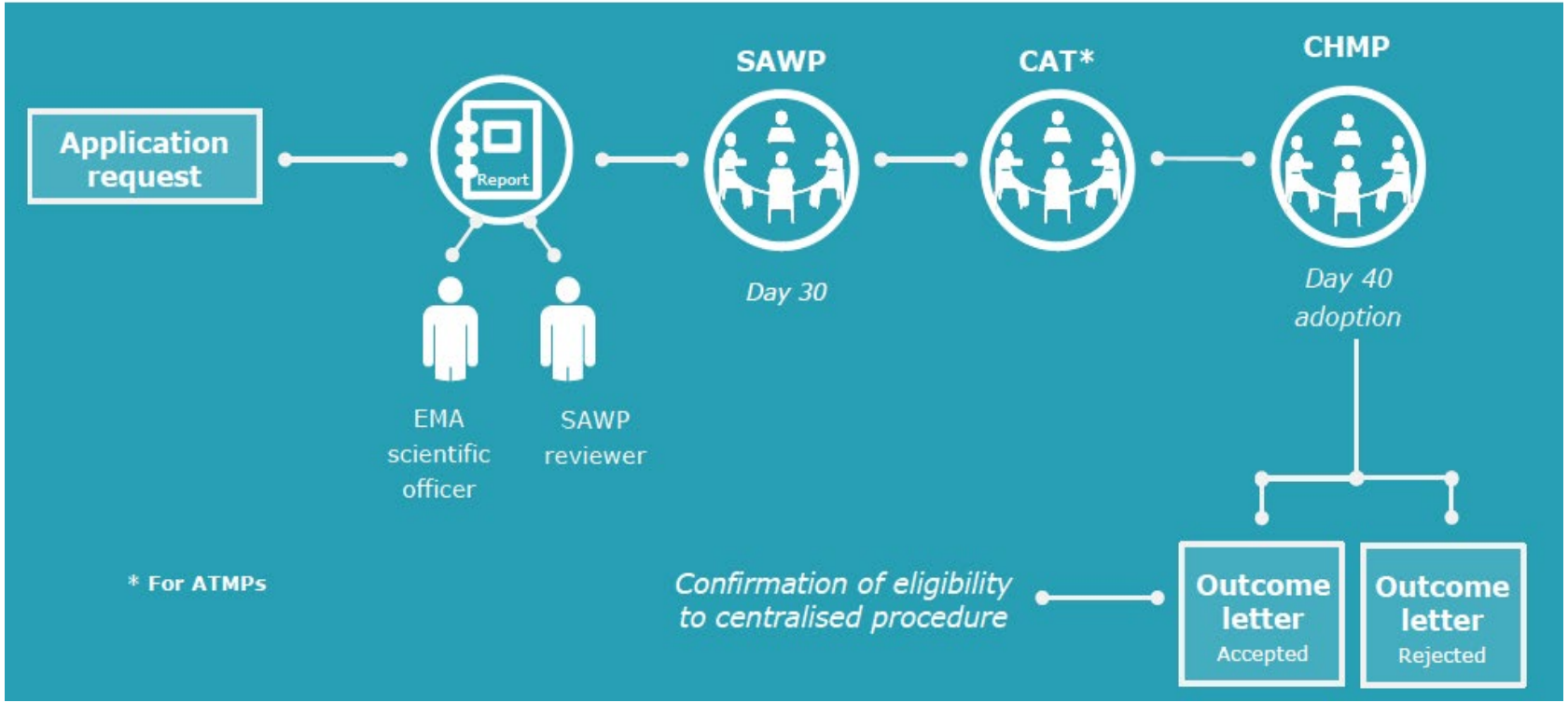
**Potential to significantly address the unmet medical need**

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

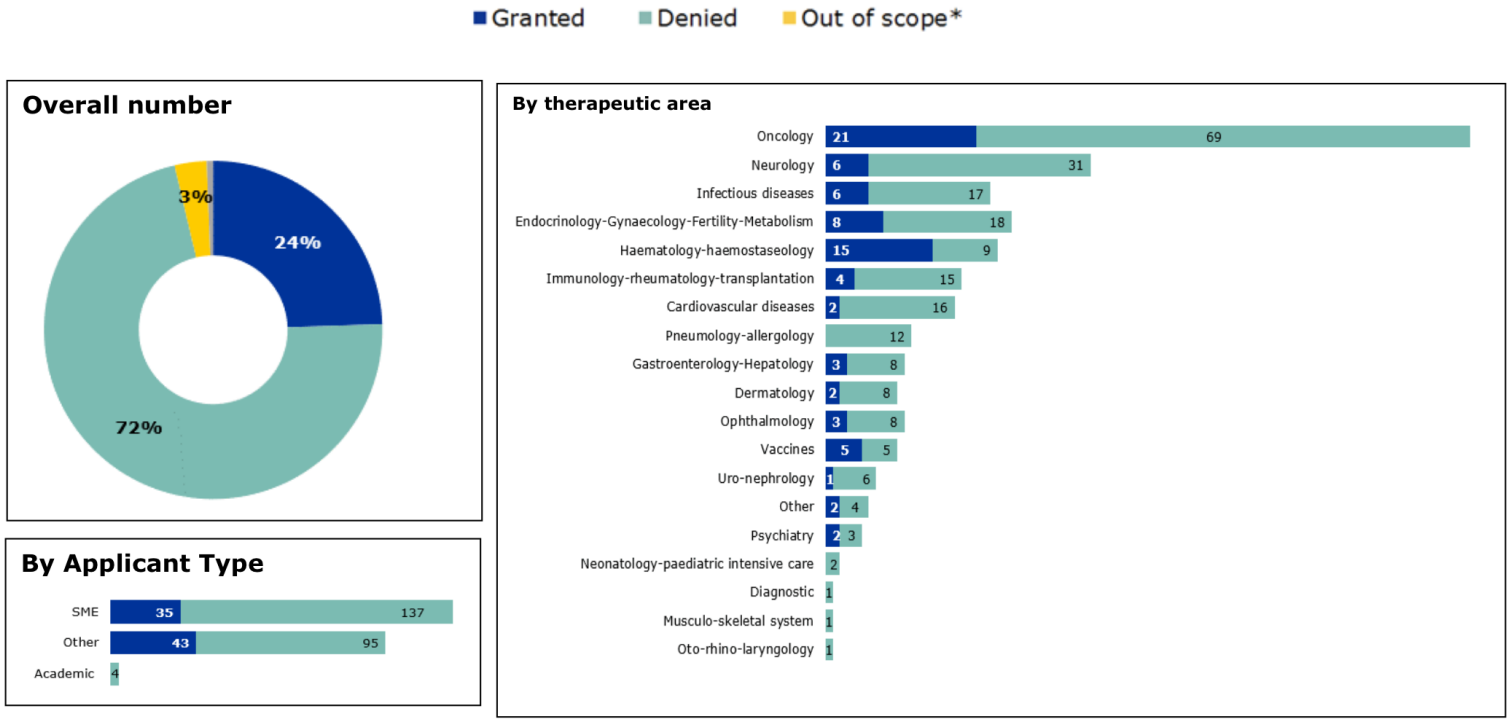
**Data required at different stages of development**

***Justification assessed by EMA's scientific committees***

# Assessment of Eligibility: 40-day procedure



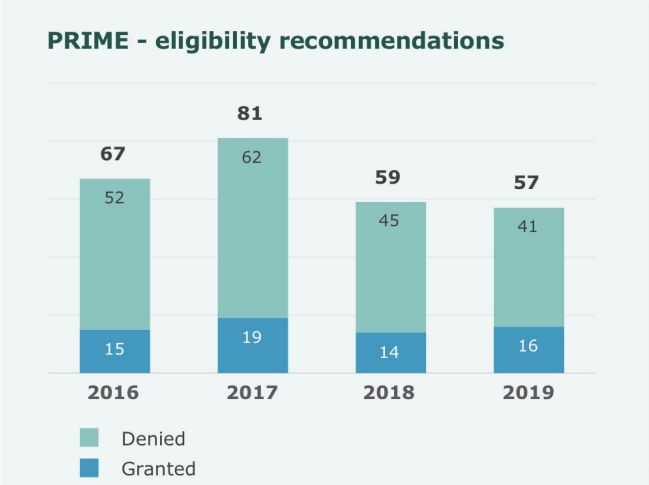
# Highlights 2016-2020 (Oct 2020)




* This indicates eligibility requests received but not started by EMA as they were deemed outside the scope of the scheme or with a format and content inadequate to support their review. These are not included in the breakdown by type of applicant or by therapeutic area.

# 310 requests for eligibility to PRIME received and assessed since launch in March 2016.

- Requests have been received in a wide range of therapeutic areas, being the majority for oncology or haematology products.
- **About 80% of PRIME products are for rare diseases**.
- **High number of requests for advanced therapy medicines, representing 40% of products granted eligibility**.
- PRIME products have received enhanced support from the Agency, with kick-off meetings organized; followed by scientific advices many including input from multiple committees as well as other stakeholders (Health Technology Assessment (HTA) bodies, patients).



# 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:

Limited relevance of ‘Proof Of Principle? data to entry

Stage of development (too early or too late)

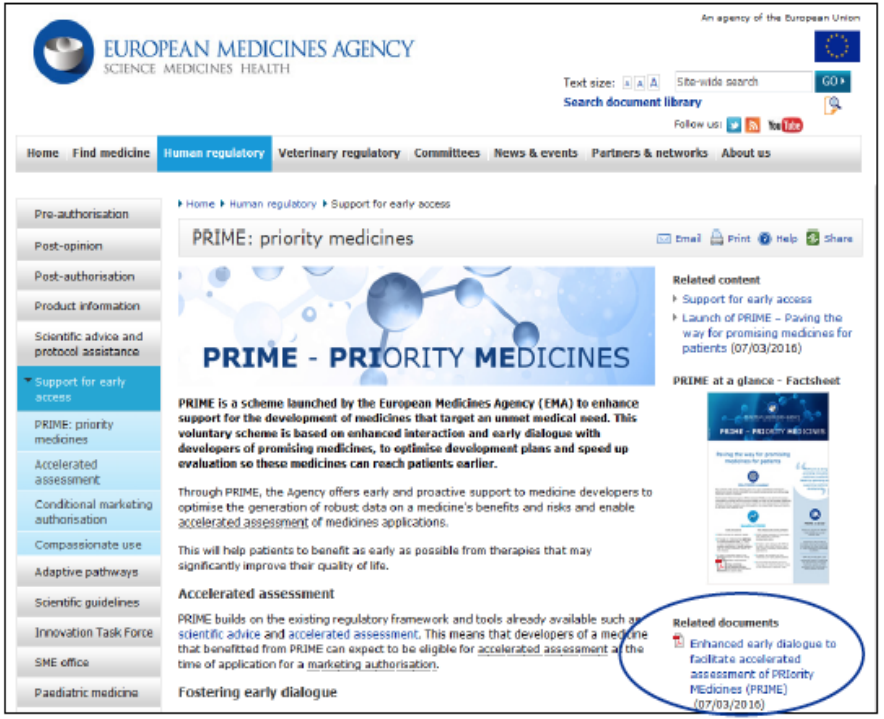
Competitor development

Identified or potential safety issues

# In summary

- PRIME aims at **strengthening support** to medicines that target an unmet medical need.
- For medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options.
- EMA will offer early, proactive and enhanced scientific and regulatory support to optimise the generation of robust data and enable accelerated assessment.
- This will allow **patients to benefit from therapies** that may significantly improve their quality of life as early as possible

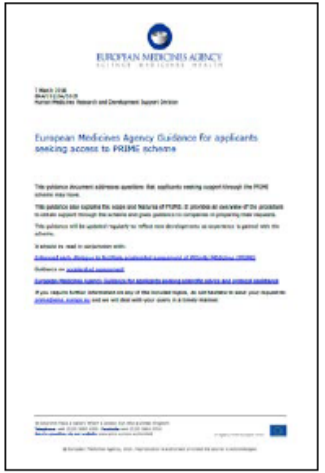
# PRIME webpage and supporting documents





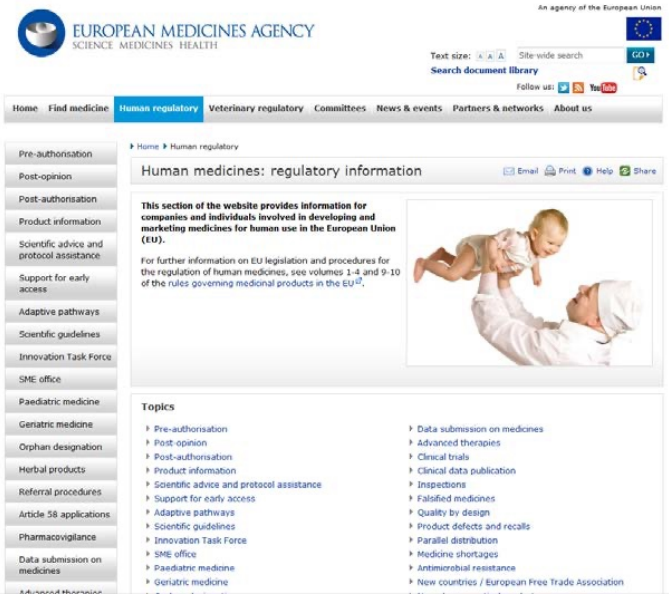
***Factsheet in lay language***

***Q&A, templates, application form for applicants***




prime@ema.europa.eu

# If PRIME is not the right tool




**EMA still can provide support through…**

# Thanks for your attention

**Acknowledgements to COMP, SAWP and EMA colleagues**