



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The PRIME scheme: experience one year on

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SME info day Supporting innovative medicines' development and early access, 17 November 2017



PRIME was launched in March 2016

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PRIME: priority medicines

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PRIME - PRIORITY MEDICINES

PRIME is a scheme launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimise development plans and speed up evaluation so these medicines can reach patients earlier.

Through PRIME, the Agency offers early and proactive support to medicine developers to optimise the generation of robust data on a medicine's benefits and risks and enable accelerated assessment of medicines applications.

This will help patients to benefit as early as possible from therapies that may significantly improve their quality of life.

Accelerated assessment

PRIME builds on the existing regulatory framework and tools already available such as scientific advice and accelerated assessment. This means that developers of a medicine that benefitted from PRIME can expect to be eligible for accelerated assessment at the time of application for a marketing authorisation.

Fostering early dialogue

Related documents

- Enhanced early dialogue to facilitate accelerated assessment of PRIME medicines (PRIME) (07/03/2016)

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PRIME - PRIORITY MEDICINES

Paving the way for promising medicines for patients

Why PRIME is needed

Many patients with serious disease have to wait only unsatisfactory therapeutic options and will often have to wait for months or even years before a new medicine can reach them.

The European Medicines Agency (EMA) developed PRIME in line with the European Commission's priorities and the common strategy to 2020 for the European medicines regulatory network. The goal is to foster research and development of medicines for patients whose diseases cannot be treated or who need better treatment options to help them live better lives.

Benefits of PRIME

FOR PATIENTS

- PRIME is driven by patient needs.
- It focuses on medicines that address an unmet medical need, or offer a major therapeutic advantage over existing treatments, or benefit patients with no current treatment options for their disease.
- It helps to translate research into the development of medicines and to bring them to the market earlier, without compromising high evaluation standards and patient safety.

FOR MEDICINE DEVELOPERS

- It helps developers of promising new medicines to optimise development plans.
- It fosters early dialogue with EMA to facilitate robust data collection and high quality marketing authorisation applications.
- It speeds up evaluation so that medicines can reach patients earlier.
- It encourages developers to focus resources on medicines that make a real difference to patients' lives.

PRIME: in brief

Medicine eligible for PRIME must address an unmet medical need.

Medicine developers must submit a request to the Agency to join the scheme, showing the potential to address the need and bring a major therapeutic advantage to patients.

EMA will provide early and enhanced support to the development of eligible medicines, aimed at their marketing authorisation and to their patients' access.

Factsheet in lay language

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 March 2016
EMA/121042/2015
Human Medicines Research and Development Support Division

European Medicines Agency Guidance for applicants seeking access to PRIME scheme

This guidance document addresses questions that applicants seeking support through the PRIME scheme may have.

This guidance also explains the scope and features of PRIME. It provides an overview of the procedure to obtain support through the scheme and gives guidance to companies in preparing their requests.

This guidance will be updated regularly to reflect new developments as experience is gained with the scheme.

It should be read in conjunction with:

- Enhanced early dialogue to facilitate accelerated assessment of PRIME medicines (PRIME)
- Guidance on accelerated assessment
- European Medicines Agency guidance for applicants seeking scientific advice and protocol assistance

If you require further information on any of the included topics, do not hesitate to send your request to prime@ema.europa.eu and we will deal with your query in a timely manner.

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Q&A, templates, application form for applicants



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

- Promote generation of high quality data
- Facilitated by knowledge gained throughout development

Building on
existing
framework;

Eligibility
according to
existing
'Accelerated
Assessment
criteria'

Eligibility to PRIME scheme

Based on Accelerated Assessment criteria

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



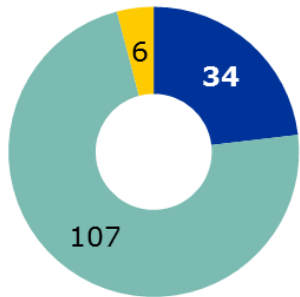
Medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation.

- Potential to address to a significant extent **an unmet medical need**
- Scientific justification, based on data and evidence available from nonclinical and clinical development

No satisfactory method or if method exists, bring a major therapeutic advantage

Introducing new methods or improving existing ones

Meaningful improvement of efficacy (impact on onset, duration, improving morbidity, mortality)



■ Granted ■ Denied ■ Out of scope*

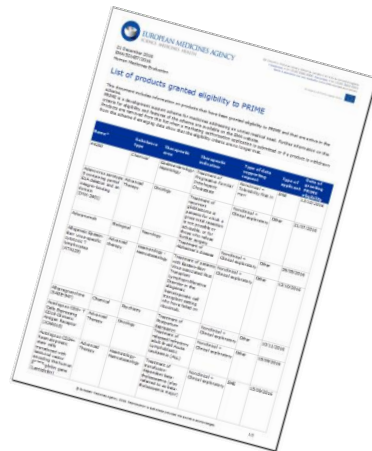
23% success rate

147 eligibility requests
34 granted*

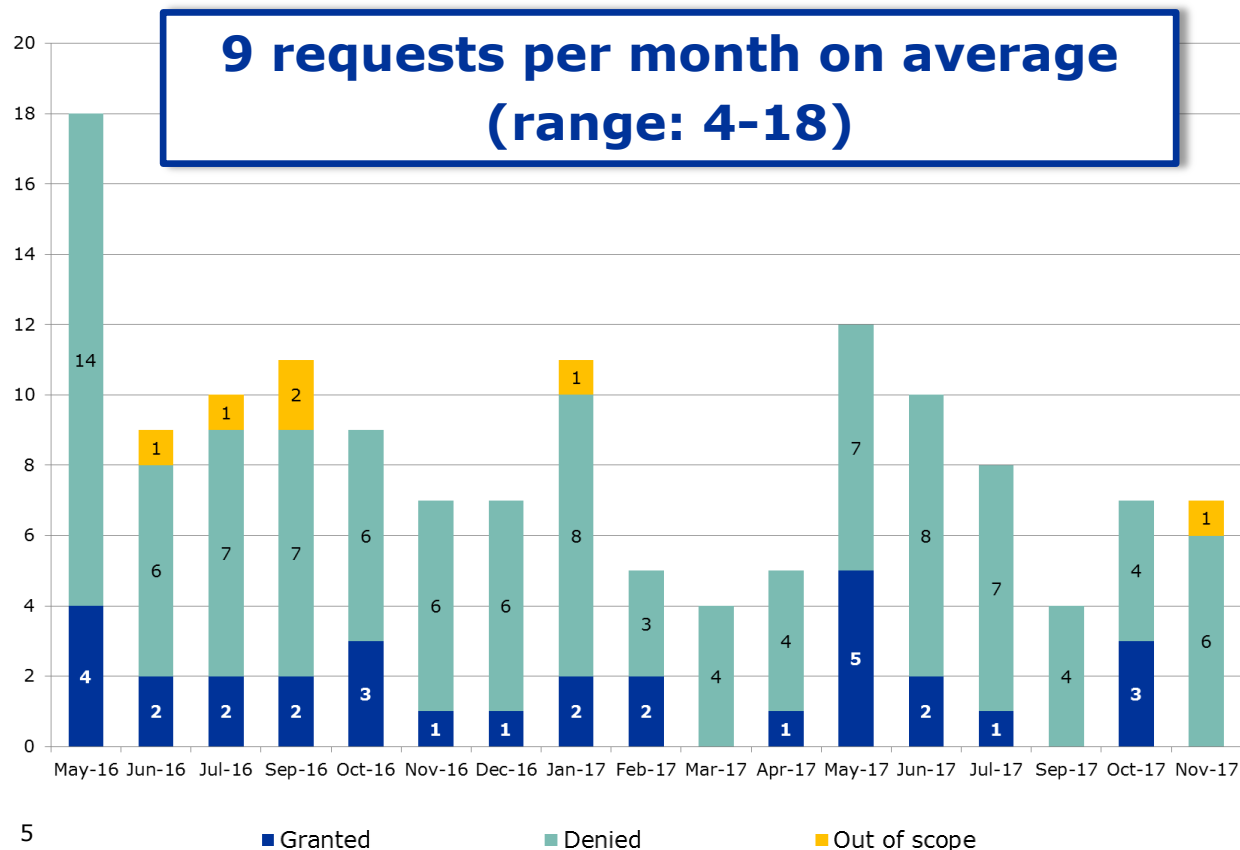
+
Publication of
report and list
of products on
EMA website

SMEs in PRIME

>50% requests received
44% of products granted



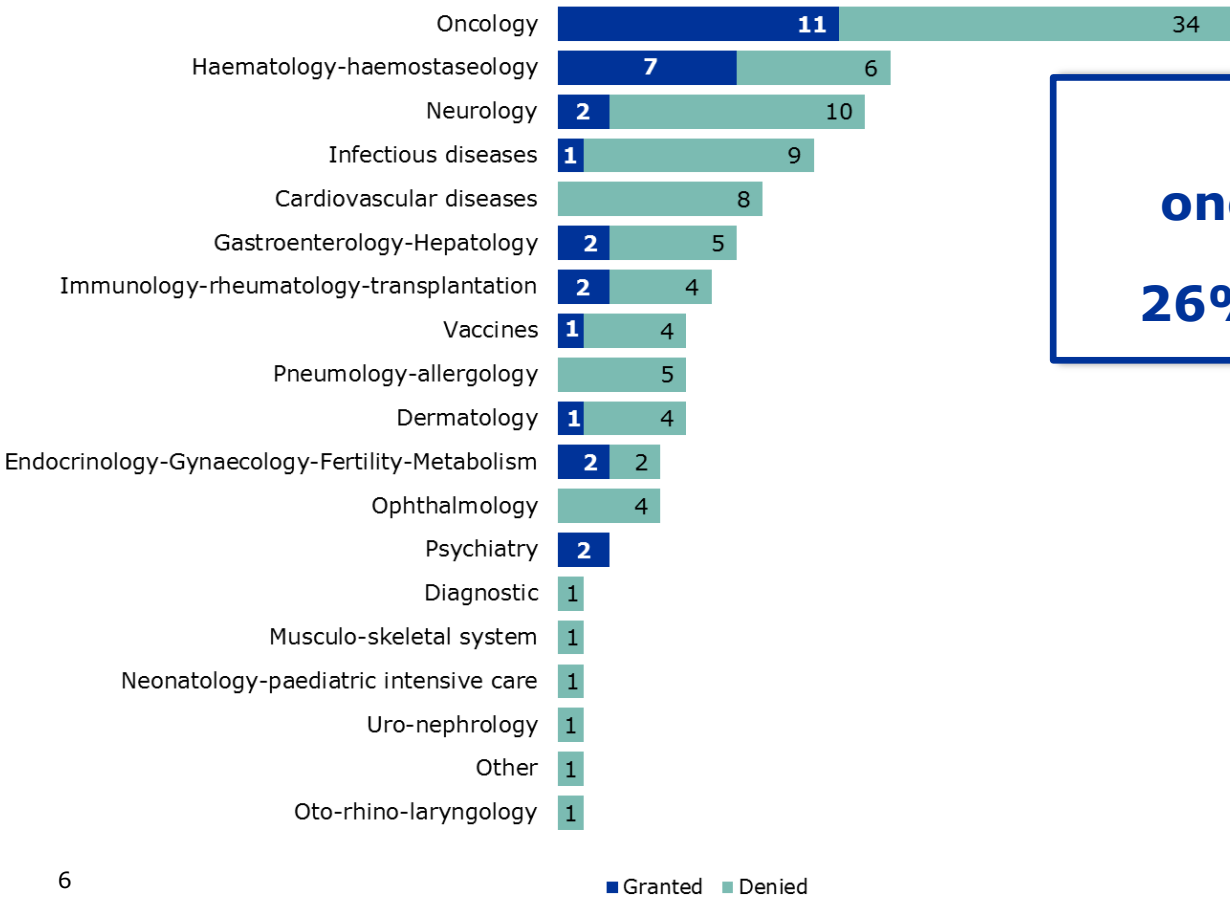
Product Name	Marketing Authorisation Holder	Therapeutic Area	Indication	Product Type	Grant Date
...	...	...	...	...	...
...	...	...	...	...	...
...	...	...	...	...	...



Good quality of applications

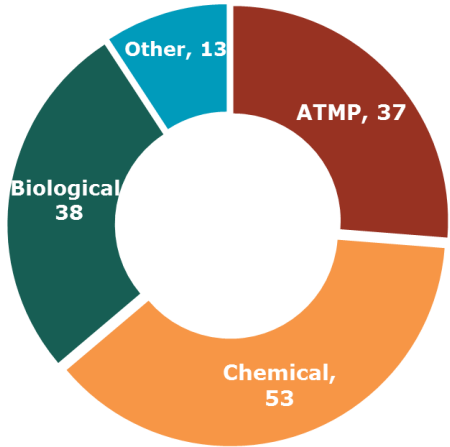
Few 'out of scope' applications

- Academic or SME with no FIM data
- Non-SME with no exploratory data
- Issue with definition as medicinal product
- Resubmission with no new data



43% requests in oncology/haematology

26% requests for ATMPs



Assessment of eligibility requests: 40-day procedure



**Short, lean process, involving multiple committees
for robust assessment**

Justification for eligibility to PRIME

1

Why there is an unmet medical need in the proposed indication

- Epidemiological data
- Description of available treatments
 - *No treatment,*
 - or*
 - *Existing treatment:*
discuss limitations and how a major therapeutic advantage could be brought



2

Data on product showing 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



Examples of Oversight group policy discussions

**Products in late
stage of
development**

Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Main focus of PRIME is to
support early in development**

**Before denying, consider
additional benefits of PRIME
for the concerned
development and type of
product**



Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Comparison to
products under
development or
evaluation**

Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Comparison to
products under
development or
evaluation**

**Other products under
development or evaluation
do not yet fulfil the unmet
medical need**



Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Comparison to
products under
development or
evaluation**

**Unmet medical
need**

Examples of Oversight group policy discussions



**Unmet medical
need**

Can be agreed:

**in *subgroup*, if clearly defined,
with mechanistic rationale for use
vs entire population**

**in *prevention* setting and
prevention of clinical complication if
relevance duly justified.**

in *non-life threatening condition*



Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Comparison to
products under
development or
evaluation**

**Unmet medical
need**

**Requests based on
literature**



Examples of Oversight group policy discussions

More acceptable at proof of principle

**Use of literature may not be
applicable similarly between
chemicals, biologicals and ATMPs**

**Need reliable, trustworthy, high
quality literature**

Applicant planning further studies

**Requests based on
literature**



Examples of Oversight group policy discussions

**Products in late
stage of
development**

**Comparison to
products under
development or
evaluation**

**Unmet medical
need**

**Requests based on
literature**

**Extrapolation of
data from other
products**

Examples of Oversight group policy discussions

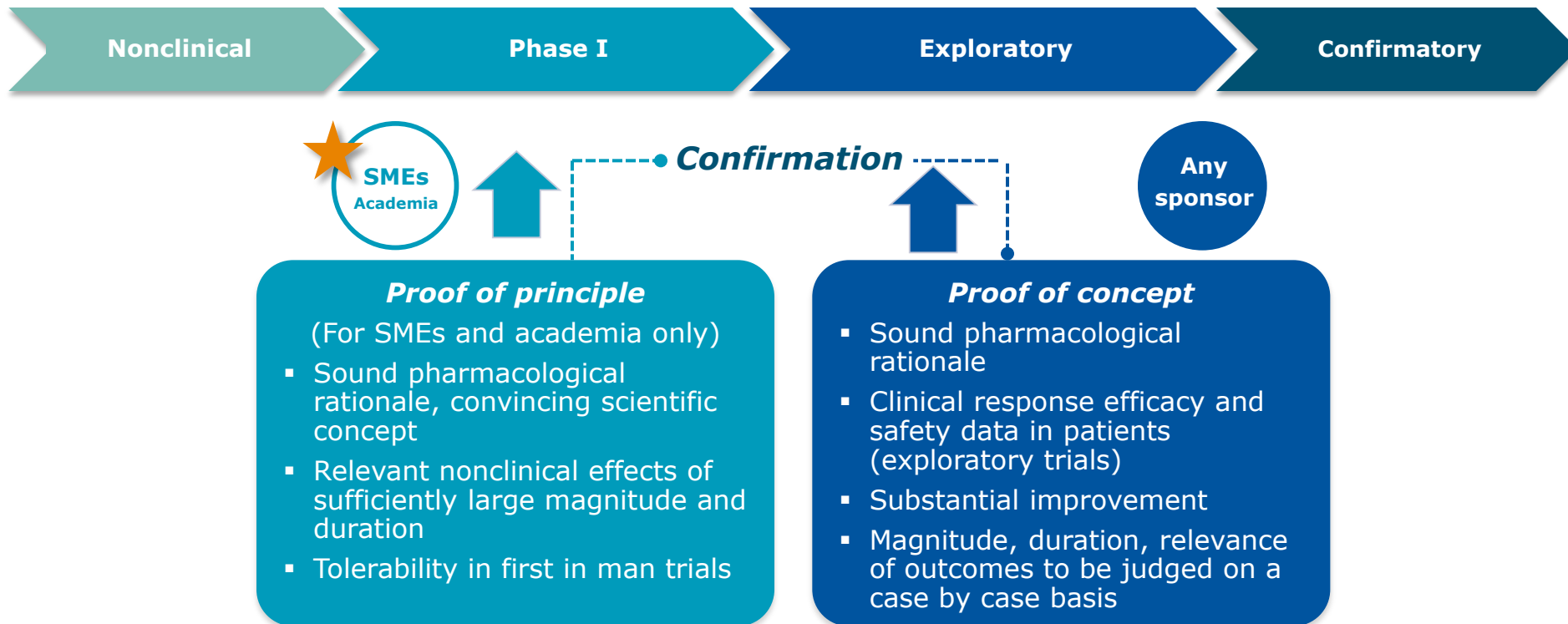
Expect data generated with the product itself

Acknowledge possibility for other products' data to be supportive (e.g. in cases with surrogate marker validated)

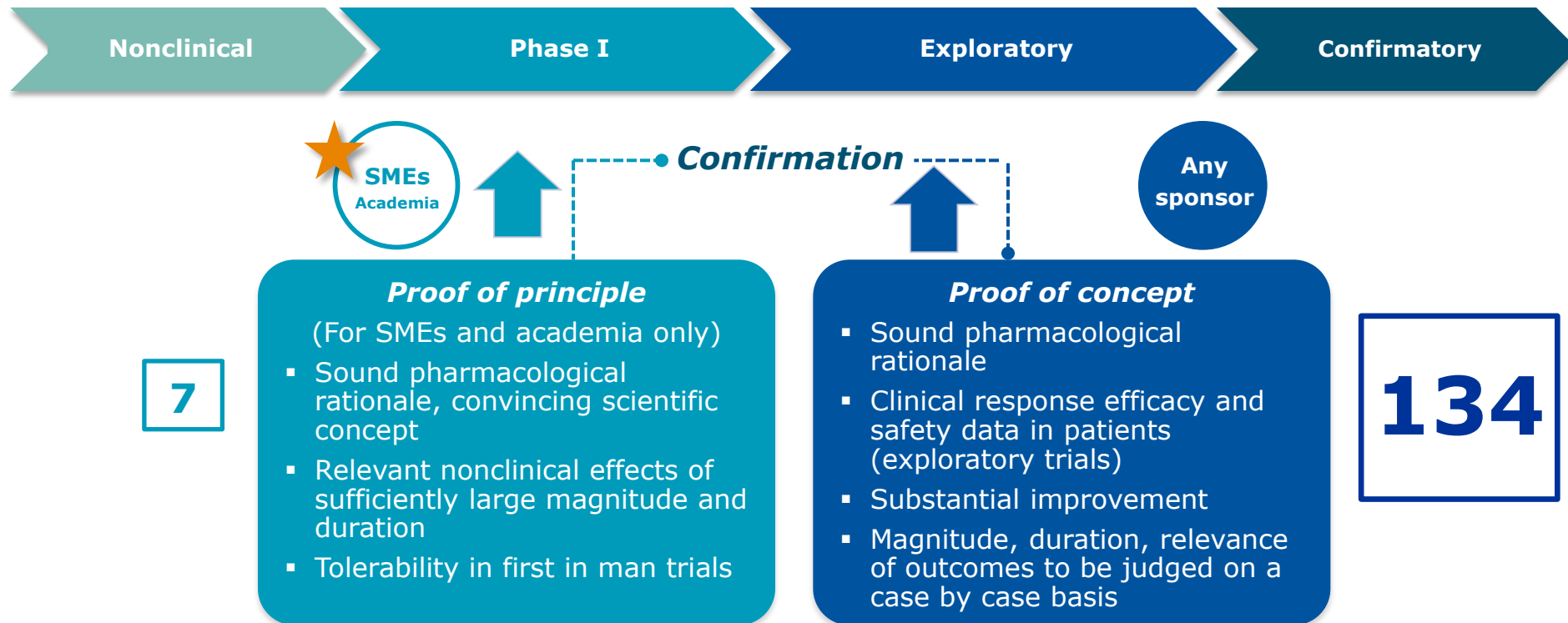
Requests based on literature

Extrapolation of data from other products

Entry points PRIME eligibility and required evidence



Entry points PRIME eligibility and required evidence



What do we expect to grant eligibility?



Unmet medical need

No treatment, or clear limitations of existing therapies (e.g. Alzheimer's disease)

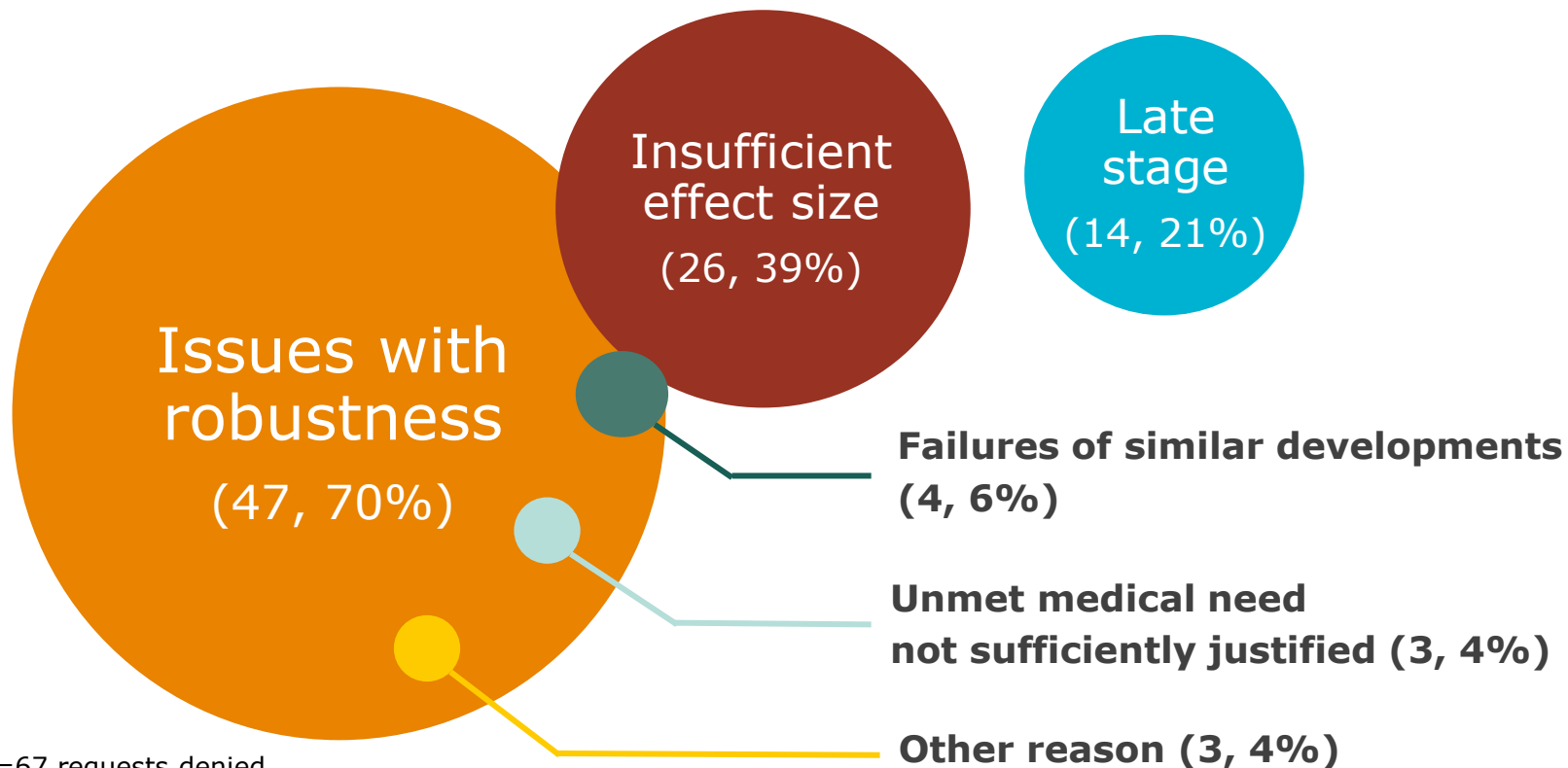
Nonclinical data supporting pharmacological rationale (e.g. gene therapy)

Clinical exploratory data on **relevant endpoint**

If uncontrolled, use **comparable historical control** i.e. need sufficient information on baseline characteristics

Magnitude of the effect size supporting major therapeutic advantage

Reasons for denial at proof of concept stage



Reasons for denial at proof of concept stage: Examples of robustness issues



Trial design issues e.g. treatment effect not isolated from other factors, use of concomitant treatments

Failed study

Inconsistency of results

across studies, study groups or endpoints

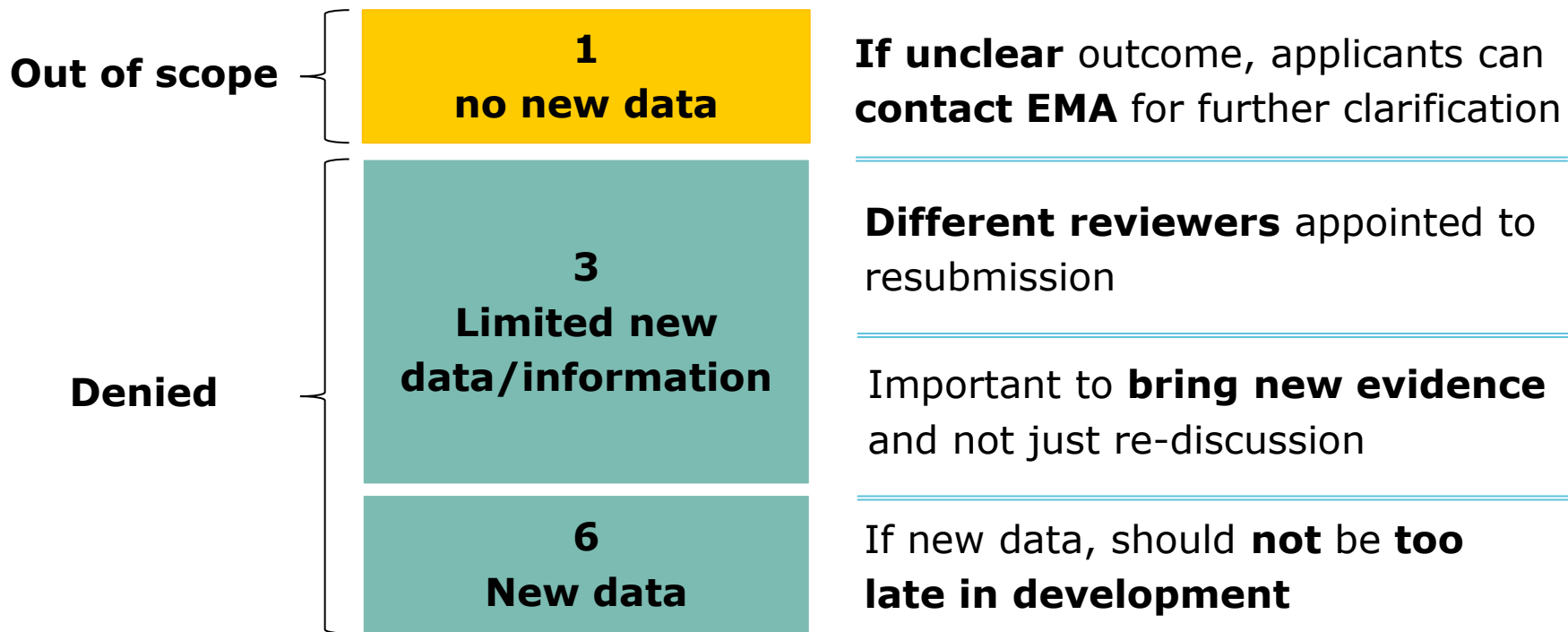
Claim in subgroup insufficiently justified

Sample issues

size, heterogeneity, insufficient information on baseline

Comparison to inadequate historical control data

10 re-submissions following denied eligibility





34 products granted eligibility to PRIME so far

21 December 2016
EMA/2107/2016
Human Medicines Division

List of products granted eligibility to PRIME

This document includes information on products that have been granted eligibility to PRIME and that are active in the scheme. PRIME is a development support scheme for medicines addressing an unmet medical need. Further information on the criteria for eligibility and features of the scheme are available on the EMA website. Products are removed from the list when a marketing authorisation application is submitted or if a product is withdrawn from the scheme if emerging data show that the eligibility criteria are no longer met.

Name*	Substance type	Therapeutic area	Therapeutic indication	Type of data supporting request	Type of applicant	Date of granting PRIME eligibility
AZD5363	Chemical	Gene therapy	Treatment of Progeria Familial Dyskeratosis (FDP)	Nonclinical + Toxicology first in man	DMB	21/10/2016
Adenovirus serotype 5 containing partial E1A deletion and an integrin-binding domain (DAX-2001)	Advanced Therapy	Oncology	Treatment of recurrent glioblastoma in patients for which a gross total resection is not possible or advisable, or for those who refuse further surgery	Nonclinical + Clinical exploratory	Other	21/10/2016
Advernavel	Biological	Neurology	Treatment of Alzheimer's disease	Nonclinical + Clinical exploratory	Other	26/09/2016
Allogeneic Epstein-Barr virus-specific cytotoxic T lymphocytes (ATN-122)	Advanced Therapy	Haematology - Hematocancerology	Treatment of patients with Epstein-Barr Virus-associated Post Transplant Lymphoproliferative Disorder in the allogeneic hematopoietic cell transplant setting who have failed on rituximab	Nonclinical + Clinical exploratory	Other	13/10/2016
Allogeneic granulocyte colony-stimulating factor (ALG-0001)	Chemical	Recovery	Treatment of neutropenia	Nonclinical + Clinical exploratory	Other	10/11/2016
Autologous CD19 ⁺ T cells expressing CD19 chimeric Antigen Receptor (CAR) (CAR-T)	Advanced Therapy	Oncology	Treatment of relapsed/refractory adult B-cell Acute Lymphoblastic Leukemia (ALL)	Nonclinical + Clinical exploratory	Other	15/09/2016
Autologous CD19 ⁺ T cells expressing CD19 chimeric Antigen Receptor (CAR) (CAR-T)	Advanced Therapy	Haematology - Hematocancerology	Treatment of relapsed/refractory adult B-cell Acute Lymphoblastic Leukemia (ALL)	Nonclinical + Clinical exploratory	DMB	15/09/2016

* Name (Medicine Agency), 2016. Reproduction is authorized provided the source is acknowledged. 1/3

- Some very innovative products with several advanced therapy medicines
- Across therapeutic areas, including rare cancers, Alzheimer's disease
- Majority in rare diseases

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.

Early Rapporteur appointment



Opportunity for **knowledge gain** on the product
Identification of **relevant expertise** and build adequate team
Opportunity to **influence** development



Very positive views on the **kick-off meeting**
✓ Importance of preparation and tailored agenda
✓ Facilitate interactions across committees and with EMA



Timing of PRIME eligibility is critical for fruitful engagement
Involvement in follow-up **scientific advice** and workload
Need to **improve follow-up communications/updates**

Kick-off meetings: experience on 22 products

Who

Applicant

CAT/CHMP/SAWP chairs

Representatives from PDCO, COMP and PRAC

Rapporteur and assessors

EMA

When

~ 4 months after eligibility

In margins of CAT/CHMP meetings

Find optimal timing, particularly if ongoing SA

How

Briefing document (~3-4 weeks in advance)

Internal preparatory teleconference (~2 weeks)

Tailored agenda

What

Broad discussion on development and regulatory strategy

Identification of issues for future scientific advices

Raise awareness on post-authorisation planning & HTA interactions

Enhanced scientific advice

12 products
20 SA requests
following kick-off meetings

Multi-stakeholder

4 EMA/HTA parallel advice
Patients involved, as applicable

Rapporteur involvement

through one of SAWP coordinator



All aspects covered

Quality,
nonclinical, clinical

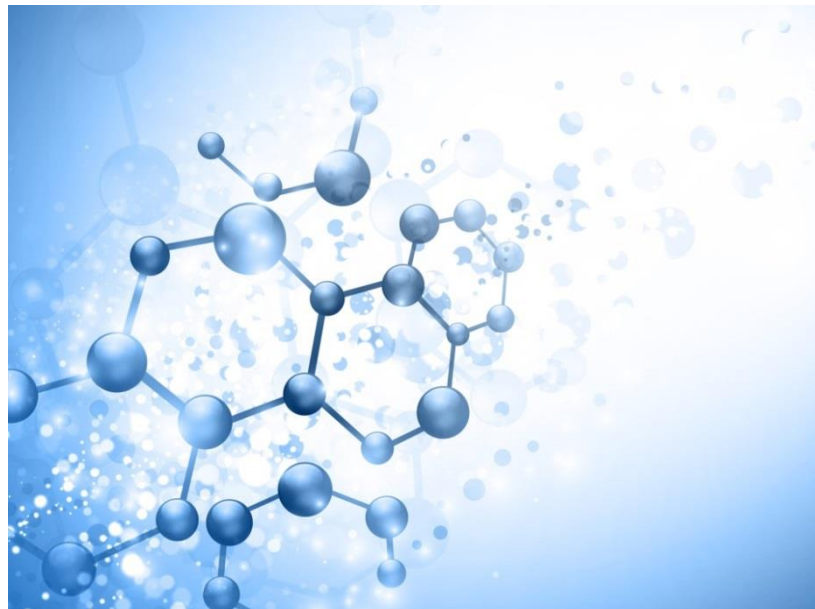
Flexibility

Shorter pre-submission
3 adopted in 40 days

Other interactions with the applicant: EMA contact point



In summary,



Eligibility review: robust, short time, in writing

Rapporteur appointment enables
early identification of potential issues

Scheme triggers discussions across product type
/ class

Excellent collaboration across committees

Iterative scientific advices with opportunity for
patients and HTA involvement



Thank you for your attention

Further information

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