One-year industry experience – *Eligibility to PRIME*

PRIME Workshop, London/EMA

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EuropaBio®
The European Association for Bioindustries

Vaccines Europe
An industry for healthy lives

This is a joint industry presentation on behalf of the trade associations shown

ebe
european biopharmaceutical enterprises

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PRIME Industry Experience

Introduction

- Provide industry reflections on experience with the PRIME scheme
  - Continuing efforts in collecting industry experience through surveys of EU Trade Associations member companies in April 2016 and May 2017
  - The most recent expanded survey collected the following information:
    - » General information / baseline
    - » Eligibility request
    - » Guidance
    - » Kick-off meeting*
    - » Overall experience / feedback*

- This presentation focuses on the initial decision to participate in the PRIME scheme and experience around eligibility.
  - Based on results of 19 companies that completed the survey
  - Survey is further supplemented with experience from individual member companies
  - Industry experience of the support within PRIME will be covered separately

*New May 2017 survey questions added to the April 2016 survey

Respondents Survey

Characteristic	April 2016	May 2017
Number respondents	6	19
Product type	--	ATMP (7) Biological (3) Chemical (8) Immunological (1)
Therapeutic area	--	Oncology (5) Neurology (5) Haematology-Hemostaseology (2) Infectious Diseases (2) Vaccines (2) Ophthalmology (1) Immunology-Rheumatology-Transplan (1) Psychiatric (1)

Feedback on guidance

General positive response in April 2016 continued to be reflected in May 2017

Document		April 2016	May 2017
Enhanced early dialogue to facilitate accelerated assessment of PRIME (EMA/CHMP/57760/20115)	Understandable/clear	4/4	18/19
	Level of detail	Sufficient (1) Not enough (1)	Sufficient (17) **Not enough (1)***
Guidance for applicants seeking access to PRIME scheme (EMA/191104/2015)	Understandable/clear	2/2	17/19
	Level of detail	Sufficient (2)	Sufficient (17) **Not enough (1)****

Specific comments:

* Guideline considered sufficient but SME office required to clarify some specific matters.

** No guidance on additional document required for submission by academia (received only after submission).

** Proposal for pre-submission interaction to discuss in detail with the agency the level of evidence expected (e.g. particularly for complex applications and in oncology/rare disease products) for entering PRIME.

Experience with applying for eligibility

General positive response in April 2016 continued to be reflected in May 2017

Document	Question	April 2016	May 2017
Deadlines for submission and timetable for assessment	Deadlines are clear	5/6	18/19
Pre-submission request form	Clear / efficient	4/5	16/19
Applicant's justification template to provide evidence supporting the request	Ease of use	(4/4)	**(17/19)****

Specific comments:

** Feedback from EMA on the level of information required in a PRIME application would be helpful

** Developmental challenges that require close collaboration with the regulators to quickly bring the product to the patient could be outlined (specific heading proposed)

** Efficiency for industry and regulators may be improved through a short summary submitted in advance of the main application to verify appropriateness of a PRIME submission (cf US Breakthrough Therapy Designation)

Trends in eligibility acceptance

- Published statistics (21 April 2017), show an acceptance rate ~19% (20 granted, 71 denied and 5 out of scope).

Characteristic	May 2017
Eligibility	Granted (8)
	Not granted (11)
Main reason for non-eligibility	No unmet medical need No major therapeutic advantage Lack of clinical data Other: • Late stage dev / no further improvements • Product had received significant previous regulatory/scientific advice
Feedback on rationale for non-eligibility	Feedback was clear (10) Not clear (1)

Trends in eligibility acceptance

- Reasons for being denied.
  - Feedback on rationale for non-eligibility

(Oncology) The CHMP rationale was **clear** however, at the time of 1st rejection the company followed advice from the decision letter and provided more data with the 2nd application, so it was a disappointment to get rejected because the product is too far advanced in development. The CHMP should be aware that oncology products (similar to rare diseases products) usually follow an accelerated development

(ATMP/Ophthalmology) **No reason given.** High unmet medical need was acknowledged by the CHMP (no treatment available), only general comments were received on the ATMP mode of action, animal model, and efficacy analysis, these were indeed the kind of matters the Company would like to discuss via PRIME.

PRIME Industry Experience

Considerations when applying

- Why companies apply to the PRIME scheme:
  - Scientific advice is a snapshot in time of a development program, whereas PRIME is voluntary scheme to ensure an early, coordinated and continuous partnering and interactions between stakeholders to optimise development plans and speed up evaluation so these medicines can reach patients earlier

- BUT, still some uncertainty in the value and considerations to be made when applying
  - On flexibility of the scheme:
    - Too narrow opportunity window between sufficient PoC data and too much regulatory advice already received – particularly in innovation areas where non-standard development is common
    - Still a more rigid process than e.g. BTD where much quicker, less formal interactions take place

PRIME Industry Experience

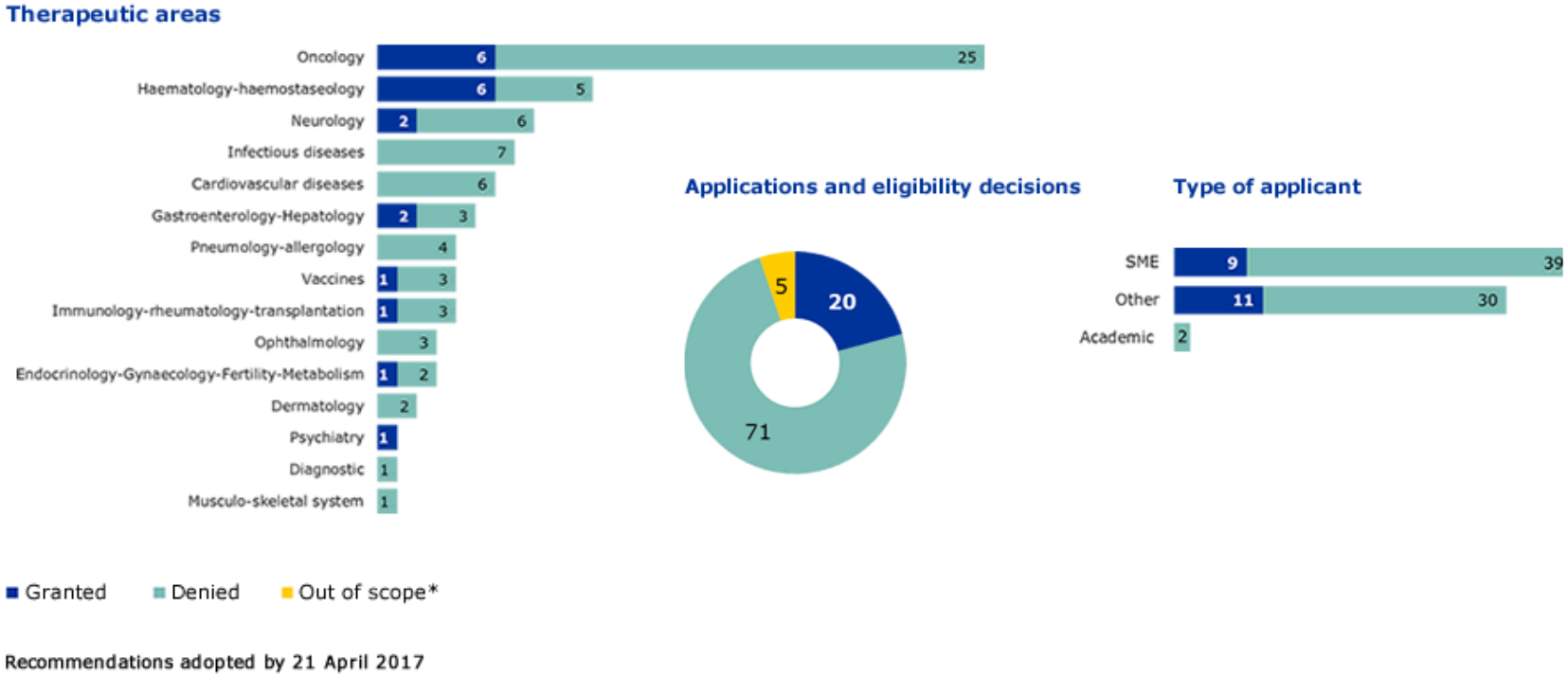
Considerations when applying

- Involvement of key actors:
  - Early appointment of Rapporteur is a key feature/advantage
    - No experience has been gathered yet on the impact of a late co-Rapporteur assignment and related transfer of knowledge and previous guidance
  - Defining role of different stakeholders
    - Stakeholders e.g. HTA bodies, WHO (they currently have no direct involvement in deciding which products go into PRIME)

- Further considerations when applying:
  - Internal pressures to manage interactions/meetings, particularly for smaller companies with parallel regulatory submissions.
  - It is new and unproven – high rejection rate (~80%), no insights regarding the criteria for selection or decision-making

Applying Eligibility Criteria

"Target conditions where there is an unmet medical need, i.e. for which there exists no satisfactory method of diagnosis, prevention or treatment, or for which the product concerned will be of major therapeutic advantage to those affected."



Certain disease areas, e.g. oncology, infectious diseases and cardiovascular diseases have a high rejection rate - further insights on trends would facilitate better understanding and decision-making in applying for PRIME (incl. out of scope)

PRIME Industry Experience

Considerations when applying - Eligibility criteria

- Some feedback interprets that the product has to be in early development to be accepted – what is the right timing in ensuring probability of success:
  - Based on experience to date, there is flexibility in the development stage of the medicines that are accepted (up to Phase III) depending on the added value PRIME scheme can bring – e.g. multiple committees' involvement, enrichment of product development
  - Narrow opportunity window between sufficient PoC data and too much regulatory advice already received – particularly in innovation areas where non-standard development is common
  - Differentiation between Proof of Principle and Proof of Concept – as a means to support small actors to be made more flexible

Conclusions

- Guidance and process around eligibility are considered clear and understandable – insights to ensure probability of success

- Extending the window of opportunity earlier for PRIME applications would enable improved and continuous alignment on priority developments in areas where clinical development may not reflect traditional approaches

- Case-by-case assessment for companies whether PRIME adds value to development program – but surrounded with uncertainties
  - 2-page summary (pre-submission interaction) to meet PRIME eligibility criteria would further help in understanding and increasing probability of success, around:
    - Therapeutic expectations regarding data package
    - Timing of application during development

- Possibility for a TC (~20 min.) in case of rejection to provide more details and clarity around the reasons for rejection - in order to support learning and consistency in the PRIME approach

Questions