EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PRIME: Implementation of recommendations based on first 5 years' experience with the scheme

8th R&D Industry stakeholder platform meeting

Presented by Stefanie Prilla and Francesca Cerreta

Agenda – Focus of implementation in 2022

- Revised entry point(s) for PRIME
- Continuity and flexibility of SA
- Roadmap of regulatory interactions & development tracker
- Submission readiness meeting

PRIME entry point

Extract from 5-year report

EUROPEAN MEDICINES AGENCY

Very few early entries in the scheme (i.e. at time or preclinical/early clinical studies) were granted (…) as it can be difficult at this stage to substantiate the promising nature of the medicine (…). Nevertheless, later entry in the scheme limits the possibility of input (…), and the opportunity for global alignment. ***If a medicine shows promise, and the need for early input is justified, the product deserves to be supported earlier, regardless of the type of developer.***

Therefore, consideration will be given to the ***best time point for access*** *to the scheme, as it might afford the greater impact on shaping development plans.*

Entry points PRIME eligibility and required evidence

Proposal in 5-year report

Any Sponsor ?

SMEs Academia

Confirmation

Any sponsor

Proof of principle

(For SMEs and academia only)

- Sound pharmacological rationale, convincing scientific concept
- Relevant nonclinical effects of sufficiently large magnitude and duration
- Tolerability in first in man trials

Proof of concept

- Sound pharmacological rationale
- Clinical response (efficacy) and safety data in patients (exploratory trials)
- Magnitude, duration, relevance of outcomes to be judged on a case by case basis → indicating substantial improvement

Entry points PRIME eligibility and required evidence

Proposal in 5-year report

- Focus on **including products early** into the scheme → opportunity to shape development
- Early entry possible based on the potential merit of the product, **irrespective of type of applicant**

Also under discussion:

- Timepoint/data requirements for entry into PRIME?
- Could we remove the need for formal re-confirmation of PRIME status at clinical PoC?
- How can we improve the support for products entering PRIME at early stages?

Flexibility of SA

Extract from 5-year report

EUROPEAN MEDICINES AGENCY

To allow for more flexibility in the provision of scientific advice in the context of PRIME, EMA will:

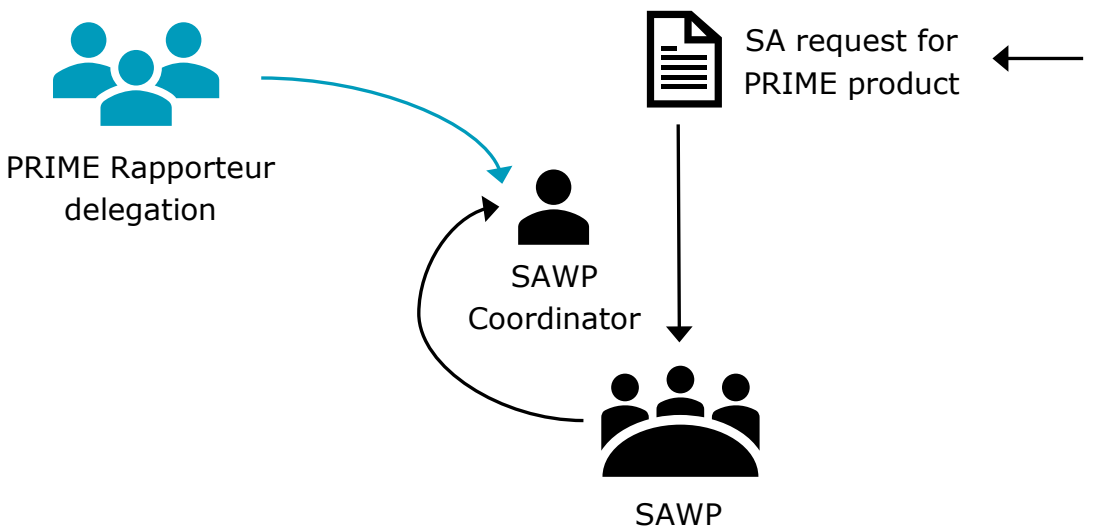
- ***build synergies with the ongoing initiatives*** *of strengthening the Scientific Advice framework, in line with EMA's Regulatory Science Strategy;*
- *Increase flexibility in a transparent manner,* ***develop guidance clarifying rules of engagement*** *with the Agency, Rapporteurs and under which situations* ***increased flexibility*** *in terms of scientific advice provision could be considered;*
- *give due consideration to the possibility of* ***regular involvement of the Rapporteur team in scientific advices****. The most appropriate experts for a given question at a given point in time should be involved. Support strong and collegial knowledge building across the network (…)*

Clarity on Rules of Engagement

- Depending on the nature of the queries by applicants/issues for discussion, can we better define **adequate level of interaction?**
  - Challenging to cover all possible scenarios, several issues may require case-by-case consideration;
  - **'Positive' list** of topics for which **SA should/must be sought**;
  - **Proposal to develop guidance on situations for (virtual) meetings** with Rapporteur and EMA product team. Examples of when such meetings are currently held: halting of trials due to safety concerns or futility, major adjustments to development plans affecting the data package to support the MAA in a significant manner, etc;
  - Possible **additional support to academic developers** and start ups.

Continuity and flexibility of scientific advice

1. Strengthen the involvement of the **SAWP Coordinator from the Rapporteur delegation** in SA requests



PRIME roadmap & development tracker

- **Roadmap of regulatory interactions**, including timing and scope of planned SAs, to be agreed at PRIME kick-off meeting
- To be kept **up-to date** by PRIME applicants as plans evolve, need for new interactions emerges

→ **Increase predictability**, thereby enabling better resource planning by PRIME Rapporteur

Continuity and flexibility of scientific advice

1. Strengthen the involvement of the **SAWP Coordinator from the Rapporteur delegation** in SA requests

2. Under discussion: Possibility/feasibility of **faster SA** in certain circumstances

Development tracker

Development tracker

- Replaces annual update in a structured easy to read manner
- Submitted and maintained **by company**
- Blueprint for PRIME KOM agenda
- Updated at regulatory interactions (SA) or ad-hoc when needed
- SharePoint link in IRIS PRIME page for EMA and network access
- Reviewed for flags when new version, and at Submission readiness meeting

TRACKER CONCEPT (to be developed)

Product name: XYZ
Last UPDATED on DD/MM/YY
PIP/waiver granted: (Y/N/Number)
Planned date/type of next interaction: MM/YY, procedure
Target quarter MAA date (if known): Q/YY

Highlight change from previous version or Flag need to discuss with rapporteur	Discussed at PRIME KOM (Y/N, NA)	SA suggested at KOM (tickbox)	IRIS SA/PIP/OD case number where issue discussed (or: planned, or NA)	FU SA suggested (tickbox)	EMA advice Followed (see drop down)	Diverges from EMA advice (Briefly explain)
GENERAL DEVELOPMENT ISSUES					Followed advice	
RCT approval challenges		☐		☐	Choose item	
HTA					Choose item Yes No, followed another agency advice No, difficulty to run study No (other reason) NA	
Payer						
Global regulatory agencies						
Registries/RWE						
Devices						
Digital technologies/AI						
Other (specify)						
I.QUALITY						
(Q1) Stability						
(Q2) Specifications						
(Q3) Manufacturing issues and process controls						
(Q4) Comparability (changes to manufacturing process / site)						
(Q5) GMP Issues						

Submission readiness meeting

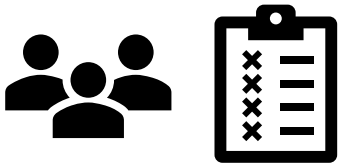
Why a 'readiness' meeting?

More than 50% PRIME MAAs start as AA but revert to standard TT

SA non-adherence rarely fully justified → MOs/OCs, delays at MAA [average of 4.2 MOs per MAA LoQ (range: 1-10)]

Industry and regulator surveys: strengthen engagement in the period between KOM and MAA

Readiness meeting ahead of MAA to ensure maturity of the application & facilitate AA



Extract from 5-year report

EUROPEAN MEDICINES AGENCY

*(…) there is room to **optimise current interactions** to support the necessary **knowledge acquisition** throughout development and thus **facilitate accelerated assessment**. Furthermore, there are currently no means for regulators to ensure that the **application is mature** enough/addresses relevant points discussed during development ahead of the submission of the marketing authorisation application.*

*A **submission readiness meeting** reviewing the **status of key development discussions** and the **implementation of advices** would strengthen the upcoming MAA assessment. It would also assess the realistic chance of obtaining and maintaining an accelerated assessment timetable by avoiding the submission of premature applications.*

Readiness meeting: Scope

To be held systematically **for all PRIME products** approx. 1 year prior to MAA filing in order to

- Discuss **status of the development** (with a focus on critical areas as per development tracker)
- Discuss **implementation of previous regulatory advice** for key development areas;
- Discuss **data package to support future MAA** and **maturity of the dossier** in view of planned type of MAA (full vs CMA vs MA under EC), incl plans for **post-marketing evidence generation**;
- Address **regulatory challenges**, e.g. ODD maintenance, PIP compliance, GMP requirements, NAS status.

Next steps

- Ongoing consultation with Committees and SAWP in July
- By Q4 2022: Update of guidance & communication
- In parallel, proposal for consultation of Industry to discuss practical aspects of the implementation, including
  - Roadmap of regulatory interactions & development tracker
  - Readiness meeting (timing, supportive documentation, etc)

Any questions?

Further information

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu/contact

Follow us on **@EMA_News**