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

8th R&D Industry stakeholder platform meeting
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
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

**Nonclinical**

**Phase I**

**Exploratory**

**Confirmatory**

Proposal in 5-year report

- **SMEs Academia**
  - **Confirmation**
    - **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

Any Sponsor

Any sponsor
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
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

   - 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)
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 \(\rightarrow\) 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
(...) 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

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