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Regulatory Science and Innovation

EIC/EMA Info Day on regulatory support for the development of innovative medicines and technologies – 31/01/2023

Questions and answers

Purpose of this document

The aim of this document is to address outstanding questions raised by the audience during the event. Questions are grouped and organised by topic.

Questions not listed in this document are questions answered by speakers directly during the event and questions on specific product for which we encourage participants to contact the European Medicines Agency (EMA) directly to discuss their query.

1. EMA support to SMEs

Information on the EMA SME Office and dedicated support to SMEs can be found on the EMA website under this link. Information on the financial advantages of SME status can be found under this webpage.

- **Can you clarify if the SME status granted by the EMA is recognized by the EIC?**

The SME status granted by the EMA is applicable solely for EMA related activities.

- **Could we use the SME incentive for translation of labelling for clinical trials?**

Translations of labelling of investigational medicinal products is not provided by EMA. EMA only provides free-of-charge translations of the product information for initial EU marketing authorisations into all EU languages (excluding Norwegian and Islandic). More information can be found here.

- **Do you have a list of registered SME consultancies?**

We do not provide a list of registered SME consultancy companies. Please consult the Public SME Register (link) to find the list of all registered SMEs. It should be noted that SME Registration by the Agency does not convey any opinion on the accreditation of a company's business activity.

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- **I have seen that we can have fee exemption for MedDRA. Can we have fee exemption for WHO Drug?**

The fee incentives for SME registered with EMA apply to EMA procedures. SME status can also be used to register in MedDRA but does not apply to any other procedure.

- **Can non-EU based companies access the SME support and incentives?**

If an enterprise is not yet legally established in the European Union (EU) or in the European Economic Area (EEA), SME incentives can be accessed through an EU/EEA-established SME regulatory consultancy. Both the regulatory consultancy and the non-EU/EEA-based company have to be assigned SME status by EMA's SME office. Further information can be found in EMA's SME user guide.

- **How often the SME status needs to be renewed?**

An assigned SME status expires two years after the date of closure of the accounts on which the declaration was based. To renew SME status, companies should submit a renewal application. Information on how to renew SME status can be found here.

- **How to request an SME briefing meeting?**

The SME office offers SME briefing meetings, free of charge, which provide a platform for a company to discuss its planned regulatory strategy at any stage of their product development. SMEs are encouraged to approach the SME office to request a briefing meeting by sending an email to SME@ema.europa.eu with background information on the product, indication, stage of development, previous interactions with regulatory authorities if any and list of questions that they would like to see addressed. The SME Office will then liaise with the company directly.

2. Priority Medicines Scheme (PRIME)

Guidance on the PRIME scheme is available in our dedicated EMA webpage. We advise you to contact the EMA directly to discuss any product specific question.

- **What's the difference between protocol assistance (ODD) and support through PRIME and how best to choose between both support mechanisms for rare diseases?**

- **What is the difference between PRIME vs EMA SA/Protocol assistance?**

Protocol assistance is the special form of scientific advice available for developers of designated orphan medicines for rare diseases. Questions can relate to any aspect of development in scope of scientific advice (e.g., quality aspects, non-clinical aspects, clinical aspects, methodological issues, overall development strategy) but also specific issues including demonstration of significant benefit within the scope of the designated orphan indication or similarity or clinical superiority over other medicines. More information can be found here.

PRIME is not an EMA procedure, it is an enhanced support scheme for the development of medicines that target an unmet medical need which can be orphan designated medicinal products or non-orphan medicinal products. PRIME relies on enhanced interaction and dialogue with a developer of a medicine to optimise the development plan and speed up access to the market.

For an orphan designated product, PRIME designation includes protocol assistance at key development milestones, but support is also be given through guidance on the overall development plan and regulatory strategy. Other key benefits such as an early appointment of the rapporteur, a 'kick-off' meeting, a dedicated EMA contact point and an early confirmation for accelerated assessment at the

time of the marketing authorisation application. Please consult the EMA website for more information on PRIME (Link).

- **Is PRIME in the EU same as accelerated approval in US?**

No, it is different.

Accelerated approval in the US is an approval mechanism that allows medicines for serious conditions that address an unmet medical need to be approved based on a surrogate endpoint.

PRIME is not an authorisation procedure, rather a support scheme to optimise development plans and speed up the evaluation of eligible medicines for unmet medical need to access the market and reach EU patients earlier. While PRIME is distinct to early authorisation mechanisms (e.g. conditional marketing authorisation), the scheme supports robust, high quality evidence generation so that those mechanisms may be utilised at the time of marketing authorisation application. The PRIME scheme support features include an early confirmation of medicines with a potential for accelerated assessment at the time of marketing authorisation application, early selection of rapporteurs from scientific committees, dedicated meeting with rapporteur and experts to provide guidance on the overall development plan and regulatory strategy and scientific advice/protocol assistance at development milestones (Link).

- **Are the eligibility criteria for PRIME the same as the ones for EMA accelerated assessment?**

PRIME eligibility criteria align with the criteria for accelerated assessment because the PRIME scheme aims to support medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation, which are products that fulfil the accelerated assessment criteria. More specifically, the criteria for assessment of PRIME eligibility (products targeting an unmet medical need, which demonstrate the potential to address this to a significant extent the unmet medical need) are the same as those for accelerated assessment. Therefore, it is expected that PRIME designated products should also qualify for accelerated assessment, but this needs to be confirmed at the time of marketing authorisation application.

- **Which dossiers is required for applying to PRIME?**

A pre-submission request form together with a justification template and literature references must be provided. Please refer to the guidance for applicants for more information (Link).

- **Is there any timeframe in which Kick off meetings are set up?**

Kick off meeting are organised as soon as possible (usually within 2 to 3 months) after the entry into the scheme with the CHMP rapporteur, relevant experts from the EU network and relevant EMA staff including the EMA contact point. Please refer to the guidance for applicants for more information (Link).

- **Is a similar procedure available for veterinary medicinal products?**

No, PRIME is for medicines for human use only.

- **Does medicinal product indicated exclusively for use in the paediatric population eligible for PRIME?**

Medicines targeting paediatric populations are eligible for PRIME in the same way as those targeting adult populations, provided they meet the eligibility criteria for PRIME.

- **Is there a point at which it is too late to apply?**
- **Regarding the entry point for very rare diseases, is it acceptable to apply for PRIME when the pivotal part of the trial is about to start/has started?**

Generally, whether a product is developed to treat a rare condition or not, the recommended entry point is at the time when exploratory efficacy and safety data is available to indicate a potential to address an unmet medical need. For products already advanced in the development programme (e.g. pivotal trial ongoing and for which scientific advice has been received), PRIME may still be granted, but the expected benefit of enhanced support through PRIME must be justified in the application, elaborating on the remaining development and post-authorisation activities for which PRIME would bring benefits.

- **Is PRIME applicable only for specific drug candidates? Or is it possible to apply for platform technologies?**

PRIME is a scheme that supports the development of new medicines only.

- **Are you sharing/discussing with FDA products with PRIME and BTD designation?**

FDA and EMA have regular exchange of information and meetings regarding breakthrough therapy designation and PRIME eligibility requests, focusing on high level topics and comparing general experience and program implementation challenges. More information can be found in the guidance to applicants, question 12 (Link).

- **Once the PRIME status is obtained, can it be reverted e.g. due to change in environment such as end of pandemic?**

Yes, a product can be withdrawn from the PRIME scheme if emerging data show that the eligibility criteria are no longer met.

- **Does PRIME cover manufacturing approach for ATMPs?**

Yes. The PRIME scheme addresses any regulatory and scientific aspect of a product development and quality aspects such as manufacturing can be part of the discussions.

- **Do you apply for PRIME per molecule or per indication in case you develop your molecule in several indications?**

The application is for a medicinal product being developed in a targeted indication.

- **Is the eligibility assessment outcome made public?**

Yes, limited information on the procedure, along with the outcome, is made public. After each CHMP meeting, an overview of the number of recommendations adopted is published in the CHMP monthly report including the type of product (e.g. chemical, ATMP), the intended indication, the type of data supporting the eligibility request (non-clinical, clinical exploratory, clinical confirmatory) and the type of applicant (SME/academic sponsor/other). For products eligible to PRIME, the name of the active substance /INN is also made public. A list of products granted eligibility to PRIME is also published and updated on a monthly basis (Link).

- **How is PRIME "connected" with the other schemes we've seen so far this morning? (ITF, SMEs incentive....)**
- **If I had a SUPPORT by ITF, will I need Also PRIME?**
- **Can an orphan drug be eligible for protocol assistance and also to PRIME?**
- **Might you clarify differences between ITF and PRIME?**

EMA offers medicine developers several opportunities for early dialogue and consultation before submitting a marketing authorisation application such as ITF, scientific advice/protocol assistance, SME office support. They are complementary to each other. The PRIME scheme is an enhanced support for a developer of an innovative product that also relies on existing EMA procedures such as scientific advice/protocol assistance.

Please also consult the EMA webpage on early development advice services that provides a consolidated list of guidance available at EMA for interactions during the development phase of a medicinal product (Link) and the info sheet on support for medicine developers (Link).

3. Orphan aspects

- **How long does it take to receive an orphan designation?**

Applications for orphan designation are examined by the EMA's Committee for Orphan Medicinal Products (COMP), using the network of EU experts. The evaluation process takes a maximum of 90 days from validation. More information can be found here.

4. Innovation Task Force (ITF)

For guidance on ITF, please consult the dedicated EMA webpage (Link).

For any product specific question, we advise you to complete the request form and send it to the ITF secretariat (itfsecretariat@ema.europa.eu).

- **How early can ITF feedback be requested?**

It is recommended to contact the ITF at the early stage of a product development, usually after proof of concept.

- **Is digital health therapy classification also within the scope of ITF?**

Informal discussions on the classification of digital health therapy, and borderline products in general, is within the scope of the ITF. However, the formal classification of a product is not within EMA's remit. More information can be found here.

- **If limited relevant guidance is available, would ITF provide feedback?**

Yes, the ITF provides feedback when guidance is not yet available due to the innovative aspects of a product/method/technology.

- **Does the ITF team or experts sign Nondisclosure Agreement (NDA)?**

All data processed within the ITF are kept strictly confidential according to the EMA's code of conduct (Link).

- **Can a research group (academia) request ITF meeting for a finished EIC project, for determining future technology/business development?**

A research group can contact the ITF to discuss scientific, legal and regulatory issues relating to the development of an innovative product/method/technology. Direct questions on business development are outside the scope of the ITF, however discussions on the development and evidence requirements for a product development may enable decision making.

- **Does the EMA also provide services for new approach methodologies to reduce animal testing?**

ITF covers the regulatory acceptance of so-called new approach methodologies (NAM) to replace the use of animals in the testing of medicines, in line with the 3Rs principles (replacement, reduction, refinement). NAMs include, for example, in silico modelling and novel in vitro assays.

- **Is the ITF only available for EU registered SMEs?**

No, the ITF is available for any developer of innovative medicines, technologies and methods: SMEs, academia or pharmaceutical companies other than SMEs, irrespective of geographical location. More information can be found here.

5. Scientific advice

Guidance on scientific advice is available in our EMA dedicated webpage (Link).

Please note that protocol assistance is the name given to scientific advice for orphan designated products. More information can be found here.

We advise you to contact the EMA directly to discuss any product specific question.

- **Does the scientific advice also cover preclinical studies?**

Yes, questions during scientific advice can indeed relate to non-clinical aspects (e.g. toxicological and pharmacological tests).

Scientific advice can relate to quality, non-clinical and clinical aspects as well as methodological issues and overall development strategy. More information can be found here.

- **Members of SAWP are nominated: what does that exactly mean? From where are they coming from?**

The SAWP is a multidisciplinary group, which comprises a chairperson and 36 members and 36 alternates coming from the EU medicines regulatory network and also includes representatives of EMA scientific committees. These members are European experts made available by national competent authorities of the EU and EEA Member States. In the nomination process, a fair representation of different areas of expertise is ensured such as pharmaceutical quality, non-clinical safety, pharmacokinetics, methodology and statistics, as well as all therapeutic fields for which there are regular requests such as cardiology, oncology, diabetes, neurodegenerative disorders and infectious diseases. More information on the SAWP's responsibilities and composition and members is available here.

- **Can UK institutions apply for EMA scientific advice?**

Yes, they can apply for EMA scientific advice.

- **If a device is being developed for delivering ATMP, can we include questions about this at EMA scientific advice?**

Yes, device questions for integral or co-packaged devices can be included in scientific advice requests. However, questions falling outside EMA's remit as medicines regulator may be rejected during the validation of the scientific advice application.

- **As biomarker provider, when is a good time point for biomarker qualification?**

As with development programmes for medicinal products, qualification advice can be requested at any time during the biomarker validation exercise leading to regulatory qualification. Early-stage scientific advice will focus on the biomarker qualification plan whereas later-stage scientific advice will also assess available data supporting the qualification, advise on further data generation studies, if necessary, and may ultimately lead to a qualification Opinion, i.e. qualify the biomarker for use in a specific context.

Of note, certification of in vitro diagnostics or companion diagnostics used to ascertain the presence or measure the levels of a biomarker is outside the remit of qualification and should follow the relevant device authorisation route.

- **How can we ask paediatric scientific advice if the only mechanism to reach the PDCO is through PIP pre-submission meeting?**

Scientific advice can be requested on paediatric aspects such as the design elements of a specific study included in a Paediatric Investigation Plan (PIP) or on combined adult and paediatric developments considering specific PIP requirements and PDCO discussions. It is the remit of the PDCO to agree the overall measures to generate evidence to support a paediatric indication while scientific advice focuses on more specific design elements. It is therefore generally advisable that an applicant has agreed a PIP before pursuing scientific advice on a paediatric development. However, scientific advice on the design of paediatric studies can be requested in advance of any PIP agreement, as long as explicit questions on the adequacy of the planned studies or of the overall paediatric development plan to support a paediatric indication are avoided. Questions relating to the adequacy of planned paediatric studies or an overall development plan to support a paediatric indication or changes to key elements of Paediatric Investigation Plan (PIP) measures and paediatrics waivers or deferrals are outside the scope of scientific advice. They need to be addressed to the PDCO via a PIP submission or paediatric procedure.

More information can be found in section 6. of the scientific advice guidance for applicants (Link).

Alternatively, the applicant may request a PIP pre-submission meeting, but this option applies to cases when the paediatric investigation plan is relatively mature and in preparation for submission to the PDCO.

- **Is Scientific Advice available & fee reductions/waivers applicable for academic sponsor?**

EMA can provide protocol assistance free of charge to academic organisations developing orphan medicines. More information can be found here.

6. Support from EMA

- **Is it possible for a company developing a project, which is going to submit a EIC proposal, to access services from EMA?**

Yes, it is possible to contact the EMA to discuss aspects relating to the development of a medicinal product for human use or veterinary use or certain types of medical devices independently of any ongoing submission with EIC.

- **What about intellectual property? Can you apply for advice before pending patents are final?**

Yes, it is possible to contact the EMA to discuss aspects relating to the development of a medicinal product for human use or veterinary use or certain types of medical devices independently of any ongoing activities related to intellectual property.

7. Medical Devices

- **Does EMA also provide advice for medical device development?**

With regards to evaluation, medical devices must undergo a conformity assessment to demonstrate they meet legal requirements to ensure they are safe and perform as intended. They are regulated at EU Member State level, with EMA involvement in certain regulatory procedures where a notified body must seek a scientific opinion from EMA before issuing a CE certificate.

A pilot project to provide scientific advice for manufacturers of high-risk medical devices by EU medical devices expert panels is currently ongoing.

More information on EMA's involvement in the medical devices area can be found here.