8 March 2023
EMA/923972/2022

Highlight report from the 9th Industry stakeholder platform on research and development support

5 December 2022

Role	Name
Chair:	Michael Berntgen
Present:	Industry: **AESGP** Christelle Anquez, Heike Wollersen, Marit Heimbürger, Oliver Hartmann, Paul-Etienne Schaeffer, Sabine Gass Ruede **EFPIA** Almath Spooner, Claudia Popp, Esteban Herrero-Martinez, Gesine Bejeuhr, Inka Heikkinen, Isabelle Stoeckert, Mireille Muller, Nadege Le Roux, Sini Eskola, Susan Bhatti, Tim Chesworth **EUCOPE** Axel Korth, Joao Duarte, Lars Hyveled Nielsen, Lucia D'Apote, Mariska Mulder, Moira Daniels **EuropaBio** Bettina Doepner, Laura Liebers, Marcello Milano, Pedro Franco, Seán Byrne **Europharm SMC** Greame Ladds, Paula Sanches **Medicines for Europe** Anabela Godinho, Beata Stepniewska , Garry Flounders, Jessica Chan, Malik Anna, Marjana Breznik, Nivedita Valentine, Ricardo Cunha, Rina Joshi **MPP Association** Andreas Emmendoerfer, Audrey Finesso, Fanny Barbotin, Jan Richter, Shayesteh Fürst-Ladani, Stephan Affolter **Vaccines Europe** Alessandro Lazdins, Maren von Fritschen, Nathalie Colinet, Solange Rohou, Stephane Callewaert, Susanne Heiland-Hunath EMA: Michael Berntgen, Alberto Ganan Jimenez, Chrissi Pallidis, Claudia Vincenzi, Falk Ehmann, Francesca Cerreta, Gunter Egger, Iordanis Gravanis, Isabel Sanchez Vigil de la Villa, Juan Garcia, Kevin Cunningham, Kristina Larsson, Marie-Helene Pinheiro, Miguel Antunes, Ralph Bax, Silvy Da Rocha Dias, Spiros Vamvakas, Thorsten Olski, Thorsten Vetter EMA scientific committees and working parties, European medicines regulatory network: Paolo Foggi, Sabine Scherer, Sylvie Benchetrit HTA bodies: Antje Behring

This was the ninth meeting between regulators and representatives of industry stakeholders to address topics of evidence generation along the medicine's life-cycle and related product-development support activities, such as scientific advice and qualification, as well as specifics for paediatric and orphan medicines. The aim of the platform is to provide an opportunity for both general updates and more focused discussions on specific processes or issues to support continuous improvement, and generally to foster a constructive dialogue with industry stakeholders.

As part of the introduction a review took place of the status of follow-up actions from the last platform meeting. Significant progress was made in accordance with the planned deliverables and timelines, and follow-up discussions took place at the 9th meeting, where appropriate.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Recent developments to address scientific advice capacity and scope

EMA provided an update on scientific advice workload and the status of procedural delays. The expected slight increase in the number of applications from previous years continued by the end of 2022, but the number showed signs of normalisation at the trail of the COVID-19 pandemic. The number of postponed scientific advice assessments has also diminished to single digits in the second half of 2022.

EMA further highlighted the update in the scientific advice briefing document template and the update in the scientific advice procedural guidance, published on 14 October 2022. The new template has a simplified structure and will be used as living document to which the regulatory assessment will be added towards the final scientific advice letter. The template has become mandatory for applications submitted with a target deadline in 2023. The updated guidance aims to clarify better the scope of EMA scientific advice which refrains from the assessment of data supporting authorisation or clinical trial applications and focuses on prospective development aspects instead. Moreover, it refrains from answering questions under the strict remit of the Paediatric Committee (PDCO), in order to avoid duplication of assessment efforts between the Scientific Advice Working Party (SAWP) and the PDCO thus achieving regulatory efficiency, while availing itself to the provision of advice on e.g. the development of paediatric formulations or the design of juvenile animal studies and paediatric clinical studies. For more detailed information, please refer to the relevant scientific advice Q&A document.

Finally, the EMA provided a first draft of a scientific advice transformation map listing the intended changes in the scientific advice process and gave an update regarding the status of other industry proposals.

FOLLOW-UP:

- EMA to involve industry stakeholders through the sounding board in the holistic mapping exercise displaying the transformation of the scientific advice offering

Closing report from the Focus group on review and strengthening the framework for qualification of novel methodologies (QoNM)

Focus group representatives provided a comprehensive summary of the work completed since March 2022. There is agreement that the QoNM platform is a key tool in Europe to confirm the validity of innovative methodologies for use in evidence generation to support benefit/risk assessment of medicinal products.

In line with the objectives set by the R&D stakeholder platform, the report covered the overview of types of methodologies for qualification in the future, the identification of procedural needs for qualification of different types of methodologies and recommendations to strengthen the QoNM process including options for expected outputs.

The FG established an overview of types of methodologies expected for qualification in the future, supported by a horizon scanning survey executed by industry trade organisations. While the survey feedback was limited, the types of methodologies identified were largely in line with expectations: biomarkers and surrogate endpoints, PROs, modelling & simulation-based methods (including for bioequivalence considerations for generics), statistical methodologies, RWE related methodologies, registries and digital health technologies (DHTs, including AI/ML based methods). Some survey

responses suggested opportunities for improving the procedural flow and shortening of procedure duration; these aspects will be taken up at the upcoming EMA multi-stakeholder QoNM workshop.

Regarding procedural needs, there was consensus that enhanced pre-competitive collaboration between developers is needed to facilitate evidence generation for Qualification. Such collaboration amongst developers and the interaction with regulatory authorities may be facilitated by new digital platforms which are currently being developed. To facilitate collaboration and avoid inefficient parallel developments there was also consensus that disclosure of Qualification Advice information could be helpful. The details of such information disclosure will need to be agreed.

Developers indicated a need for guidance and facilitation to qualify additional contexts of use or broader contexts of use of a qualified methodology. Given that considerations regarding the evidentiary requirements for different contexts of use are highly case specific, it was acknowledged that for the time being Qualification Advice interactions are the best way to discuss and agree additional evidence requirements. A need for life-cycle management of qualified tools was acknowledged; how this could be operationalised will require further consideration and discussion.

With a view to methods utilising technologies which are not within the immediate EMA remit, it was suggested to explore options to involve suitable experts as members of the EMA Qualification Team. It was also agreed need to keep available procedural guidance updated, to standardise the layout of published outcome documents and improve the publication of QoNM related information. Members of the Focus group will act as sounding board for the EMA workshop preparation and the development of the proposals to optimise the qualification framework after the EMA workshop.

FOLLOW-UP:

- EMA to organise a multi-stakeholder workshop on the qualification framework in 1H23
- Members of the previous Focus group to act as sounding board for the workshop preparation and the development of the proposals to optimise the qualification framework

Progressing parallel Joint Scientific Consultations

EMA and EUnetHTA21 provided an update on the status of parallel Joint Scientific Consultations (JSC) by regulators and HTA bodies. An overview of the selected products during the last two open calls was presented. The most recently adopted guidance documents were revisited. An overview how the relevant milestones in the HTA-Regulation are expected to be achieved before full applicability of the HTA-Regulation completed the overview. EMA and EUnetHTA21 reported on their efforts exploring possibilities for requests for advice to be submitted between September 2023 and December 2024.

During the discussion stakeholders highlighted their continued interest in EMA and HTA bodies accepting requests for advice before the HTA Regulation becomes applicable. The application of selection criteria was discussed as well as the potential for capacity building in the network.

FOLLOW-UP:

- EMA and EUnetHTA 21 to continue exploring opportunities for parallel consultation in the gap period after the consortium finishes and before the new HTA Regulation comes into application

Implementation of the recommendations from the PRIME 5-year review

In follow-up to the discussion at the 8th Industry stakeholder platform on research and development support in July 2022, EMA presented the current status of the implementation of the recommendations arising from the analysis of the first 5 years' experience with the PRIME scheme, which have been developed in consultation with Industry representatives and following agreement with the Committees, Scientific Advice Working Party (SAWP) and other governance bodies.

In relation to ensuring greater continuity and flexibility in the provision of regulatory/scientific advice a new pathway for expedited Scientific Advice for PRIME developments was presented, in cases where more urgent CHMP advice on specific elements of development is required. Stakeholders presented feedback in support for these PRIME initiatives, emphasising the need for flexible and rapid dialogue with SAWP and Rapporteurs.

In the context of optimising the current interactions and knowledge sharing through the duration of the PRIME scheme, the details and structure of a submission readiness meeting (SRM) ahead of the marketing authorisation application was presented to review the status of key development aspects and the implementation of previous advices, with the ultimate aim to ensure applications are sufficient to obtain and maintain accelerated assessment. Stakeholders welcomed the initiative to support more predictable AA, emphasising the importance of identifying the scope and correct window of opportunity to discuss and resolve outstanding issues in the SRM.

To increase transparency of applicants' plans for regulatory interactions, EMA also presented details of the PRIME development tracker which will be used to track and update regulators on the development, and to support Kick-off meeting and submission readiness meeting discussions. The document aims to focuses on key aspects of development to provide a high-level overview for regulators while minimising administrative burden for medicine developers. Stakeholders presented feedback, including the need to balance the value of tracker with administrative burden, and for clear guidance on the requirements for filling and maintain the tracker.

FOLLOW-UP:

- EMA to finalise the development tracker template taking industry comments into consideration, for 1-year piloting from 1Q23
- EMA to develop guidance for an expedited scientific advice procedure, with involvement of the existing sounding board, for launch in 1Q23
- EMA to further refine the planning and conduct of submission readiness meetings in 1Q23, with involvement of the sounding board

Delivery of the EMA/EC Paediatric Action Plan

The main achievements of the EMA/EC action plan on paediatrics were presented. The plan had been agreed in 2018 following a multi-stakeholder workshop at the EMA to address challenges identified by the European Commission's ten-year report on the implementation of the Paediatric Legislation. The agreed actions have been achieved through collaboration of all stakeholders. Among other things, the action plan has led to a strengthened focus of paediatric developments on areas of unmet medical needs, improved cooperation of regulators and other stakeholders, better utilisation of innovative methodologies (e.g., extrapolation) and to reduced bureaucracy in the handling of PIPs. A closing report with a detailed overview of all achievements will be published in early 2023, together with guidance on the new concept of a "stepwise PIP", which is one of the key deliverables of the action

plan. It is expected that the actions taken will increase the efficiency of paediatric regulatory processes under the current legal framework. Moreover, learnings from the action plan are expected to be translated into the ongoing revision of the paediatric legislation.

FOLLOW-UP:

- EMA to publish the closing report of the EMA/EC paediatric action plan

Closing report from the Focus group on the practical application of principles relevant for the PIP framework

The objective of this group was to develop further the principles that were established in the Focus group on the concept of an 'stepwise' (previously known as evolutionary) PIP (sPIP) to guide the practical application. The primary focus was on the sPIP concept; furthermore, discussions on key elements (KE) for a PIP in general should be matured to support a review of the applicable guidance with focus on a development concept rather than a study protocol.

An overview of the outcome of the Focus group discussions was presented. The group has developed a guidance document for the "stepwise PIP process" to be used in the pilot phase, which will be launched in the first quarter of 2023. The guidance includes the general principles and an outline of the scope of the sPIP and information on the practical steps for submission. In addition, the group worked on updating the key elements form which forms the basis of the PIP opinion. The key principles of the updated form are to update the format of the template to resemble the agreed opinion; removal of repetition and unnecessary detail; and possibility to update contingent measures as data are generated via modification procedures.

FOLLOW-UP:

- EMA to implement the new Key elements template from 1Q23
- EMA to publish the guidance for the pilot phase of the stepwise PIP process
- Members of the previous Focus group to act as sounding board for the finalisation of the sPIP guidance and the preparation and evaluation of the pilot

Changes to the Paediatric Annual Report preparation

In the context of the current requirements of the Paediatric Regulation, an optimisation of the process for the preparation of the Annual Report to the European Commission has been implemented. The objective is to ensure a consistency in the evaluation approach, to achieve clear conclusions and to improve communication. The initial changes focus on the operational aspect of confirming compliance of the timing of PIP submission through early interactions. This will be documented in the summary report. The next steps of the optimisation process will deal with other aspects of the Annual Report, including the requirement to place on the market medicinal products authorised for a paediatric indication following completion of an agreed Paediatric Investigation Plan.

FOLLOW-UP:

- Industry stakeholders to be consulted on the planned updates regarding the Article 33 reporting in the Annual Report, once developed further

Expert panels scientific advice to medical device manufacturers provided by the Expert Panels

As announced at the Industry Standing Group meeting in November 2022, EMA will launch a scientific advice pilot for medical devices in early 2023. The advice will be provided by the Expert Panels to medical devices manufacturers on their clinical development strategy or proposals for clinical investigation regarding class III devices or class IIb active devices destined to administer and/or remove a medicinal product.

The medical devices to be prioritized for the pilot phase include: 1/ Breakthrough devices for unmet medical needs (defined in MEDDEV 2.7/1 rev.4, Appendix 8 as devices for medical conditions that are life threatening or cause permanent impairment of a body function and for which current medical alternatives are insufficient or carry significant risks); 2/ Devices intended to benefit a relatively small group of patients in the treatment or diagnosis of a disease or condition, 3/ Novel devices with a possible major clinical or health impact.

A group of five members from the Expert Panels will be constituted based on their expertise, availability, and absence of conflict of interest for each procedure. Every scientific advice will start with a pre-submission meeting to guide the applicant on the drafting of the supporting documentation as well as to get an initial view of what are the clinical development main issues. The experts will have 60 days to assess the documentation once it is provided by the manufacturers and to address their questions.

During the pilot phase no fees will be requested from the applicants, but this will be limited to a maximum of 10 scientific advice requests, divided in two selection periods in 2023. Small and Medium size Enterprises (SMEs) are encouraged to participate during this pilot phase.

Progress with the development of a pilot for scientific advice on drug-device combinations

As a follow-up to the discussions at the 8th Industry stakeholder platform on research and development support in July 2022, industry presented their in-depth analysis of scope/remit for scientific advice on Drug-Device combinations and Drug-Companion Diagnostic combinations, including typical types of questions that would be subject to such advice. From a developer's perspective there is growing combined use of medicinal products with medical devices (including software) as well as companion diagnostics, which results in complexities due to different regulatory frameworks.

Seeking a pragmatic approach to facilitate discussions on evidence generation plans, the proposal from industry was to explore opportunities to enable dialogue between EMA and developers to identify the most appropriate path forward. It was also clarified by industry that further to the need for scientific advice there are also regulatory and procedural related questions, which however need to be dealt with separately involving the relevant decision makers and stakeholders.

Initial discussions took place what could be the scientific questions in such development programmes, and which type of expertise would be needed. To progress these reflections further, it was agreed to set up a dedicated Focus group on provision of scientific advice for medicinal product developments comprising of drug-device combinations and drug-companion diagnostic combinations.

FOLLOW-UP:

- Establishment of a Focus group to develop such pilot on the basis of the detailed analysis and exemplary use cases provided by industry stakeholders; need to involve other stakeholders responsible for medical device activities in these discussions

Follow-up on strengthening patient-centric development

EMA reported back on the outcome of the recent multistakeholder workshop to advance on the generation and use of patient experience data (PED). It is acknowledged how users of medicines become instrumental in helping to optimise medicines development and regulatory decision-making. Although there has been much progress in the EU in recent years, PED are still not systematically included in all aspects of medicines development and regulation

Reinforcing patient relevance in evidence generation is a key priority in the EMA's Network Strategy and the Regulatory Science Strategy. A multi-stakeholder approach is needed for defining robust and meaningful PED for medicine's development and regulatory decision-making. Robust methodology needed to capture and analyse what matters most to patients, to optimise medicines development, regulatory decision-making and HTA assessments. In this respect, EMA agreed to work on a reflection paper on the best EU approach to generate and collect PED.

EMA also reported from the experience from a CHMP pilot involving patients early during evaluations of new marketing authorisation applications. The results of the pilot are very positive, and it is agreed to continue with early involvement of patients and to explore extending practice to involve healthcare professionals.

FOLLOW-UP:

- EMA to develop an action plan as follow-up from the workshop and identify opportunities for engagement with stakeholders, including industry, such as contribution to the reflection paper