5 October 2023
EMA/326290/2023

Highlight report from the 10th Industry stakeholder platform on research and development support

11 July 2023

Role	Name
Chair:	Michael Berntgen
Present:	Industry: **AESGP** Klavdija Kmetič, Mike Picchioni (Topic 8) **EFPIA** Tim Chesworth, Sini Eskola, Esteban Herrero-Martinez, Angelika Joos, Nadege Le Roux, Mireille Muller, Claudine Sapede, Isabelle Stoeckert, Alan Morrison (Topic 5) **EUCOPE** Lucia D'Apote, Joao Duarte, Bertrand Fournier, Lars Hyveled-Nielsen, Axel Korth, Marcello Milano **EuropaBio** Francesca Buttigieg, Kara Daly, Pedro Franco, Alexa Hunter **Europharm SMC** Parminder Kaur **Medicines for Europe** Susana Almeida, Przemysław Reszka, Martin Schiestl, Elisabeth Kapeller (Topic 8) **MPP Association** Fatima Bennai-Sanfourche, Astrid Cornee, Andreas Emmendoerffer, Shayesteh Fürst-Ladani, Mateja Ravnikar, Mike Wallenstein **Vaccines Europe** Bart Barefoot, Maren von Fritschen, Tiago Fonseca (topic 3), Gloria Garcia-Palacios (Topic 6). EMA: Stiina Aarum, Ralph Bax, Michael Berntgen, Kevin Blake, Kevin Cunningham, Roberto De Lisa, Corinne De Vries, Maria Filancia, Iordanis Gravanis, Anna Gross, Thorsten Olski, Chrissi Pallidis, Marie-Helene Pinheiro, Thorsten Vetter. European Commission: Valentina Barbuto, Marco Capellino, Rainer Edelhaeuser, Paul Piscoi. EMA scientific committees and working parties: Brian Aylward, Sylvie Benchetrit, Pierre Demolis, Paolo Foggi, Jörg Engelbergs, Sheila Killalea, Andreas Kirisits, Ilona Reischl, Sabine Scherer, Hilke Zander, Joerg Zinserling. HTA bodies: Stephanie Said. Notified bodies: Theresa Jeary, Alex Laan, Jonathan Sutch.

This was the tenth 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

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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.

Update on latest developments in scientific advice

EMA advised on an upcoming update of the scientific advice public guidance consisting of removal of outdated information, re-structuring and consolidation of existing information. These changes should enhance the reader-friendliness of this guidance. Industry representatives welcomed the upcoming changes which address previous industry comments and reiterated the need for publication of track-changes versions of key guidance documents allowing easy identification of changes in the latest version (post-meeting note: the update was published on 31/07/2023; please refer to the main scientific advice webpage: Scientific advice and protocol assistance | European Medicines Agency (europa.eu) and secondary webpages to it).

EMA updated on the status of the start of scientific advice procedures. Previously reported delays have practically ceased to exist since beginning of 2023, facilitated by lower numbers of applications in the first half of the year. It was clarified that the October 2022 guidance update relating to paediatric scientific advice was not a major contributor to reduced applications; industry representatives noted the perceived reduction in opportunities for discussion meetings as part of the scientific advice process as a possible reason. Industry associations may consider conducting a survey to better estimate the expected volume of scientific advice applications.

Finally, EMA presented an updated version of the scientific advice transformation map, highlighting briefly the three pilot initiatives related to PRIME, the Focus Group regarding scientific advice on drug-device and drug-companion diagnostic combinations, early work in the ACT-EU Priority Action 7 on a consolidated scientific advice process ahead of clinical trial applications also meant to serve the requirements of marketing authorisation and the upcoming review of the framework for Qualification of Novel methodologies which will start in follow-up the relevant workshop held in April 2023. The Agency further informed on ongoing initiatives to build IT tools allowing easier knowledge sharing both within the Agency and in the wider EU regulatory network. On the topic of knowledge management, industry representatives expressed a desire to understand better the access to information from various regulatory submissions by regulatory assessors with various roles and to discuss how fragmentation both within and outside the regulatory network can be minimised while preserving confidentiality standards. The topic will be further discussed in the scientific advice sounding board.

FOLLOW-UP:

- Discussion on opportunities for dialogue in the context of scientific advice, including criteria for and objectives of discussion meetings as well as do's / don't's, initiated by EMA together with SAWP and brought to the sounding board
- Continue dialogue through the sounding board with focus on better understanding the trends for scientific advice requests (industry to consider survey), knowledge management (industry to identify scope) and the transformation map (EMA to maintain)

Progress with the implementation of the recommendations to further strengthen the PRIME scheme

EMA presented an update on the newly launched features of PRIME support, arising from the recommendations of the analysis of the first 5 years' experience with the scheme. The new features were launched as pilots in March 2023 following agreement with the Committees, Scientific Advice Working Party (SAWP) and other governance bodies, and in consultation with industry representatives.

EMA presented details of the finalised pilots for expedited Scientific Advice for PRIME developments, the submission readiness meeting (SRM) ahead of the marketing authorisation application, and the PRIME regulatory roadmap and development tracker. EMA summarised the preliminary experience of each feature to date, including the assessment of the criteria for the first requests for expedited scientific advice, and observations following the first submissions of the new development tracker. EMA outlined plans to gather feedback on the developers' and regulators' experience of the pilots through questionnaires. This feedback will in turn be used to analyse, refine and further improve the features going forward. Stakeholders welcomed the launch of the pilots and the opportunity to provide input into the development of questionnaires to analyse the pilots.

EMA also presented an overview of the updated PRIME guidance to applicants and webpage, which provides guidance on the new pilot features and simplifies and streamlines the existing guidance for developers considering a PRIME application and for developers with products in the scheme.

Finally, EMA presented an overview of the launch of PRIME activities in IRIS. The onboarding is stepwise, with launch of the PRIME eligibility application, along with processes for transfer/withdrawal of the PRIME designation, in July 2023. Additional features to support PRIME meetings and the submission of periodic development updates will follow in September 2023.

FOLLOW-UP:

- EMA to consult with the sounding board when developing the questionnaires to analyse the pilots
- Trade associations to cascade information on the onboarding of PRIME onto IRIS based on already published material, as well as subsequent procedures to be onboarded ("PRIME meeting request" and "PRIME Periodic update submission") once published

Report from the multi-stakeholder workshop on qualification of novel methodologies (QoNM)

EMA provided a preliminary overview of considerations which have emerged during the multi-stakeholder workshop on futureproofing the Qualification of Novel Methodologies (QoNM) platform in April 2023. A workshop report is being drafted and an action plan will be developed, on which the industry sounding board will be consulted before implementation.

Industry also presented a read-out confirming that workshop discussions have been helpful and rich in content, showing that Qualifications are enablers to innovation and foster an innovation friendly ecosystem by allowing scientific debate on new tools and technologies. Commitment to continuing the work on futureproofing the QoNM procedure in sounding board consultations was expressed.

FOLLOW-UP:

- EMA to publish the report from the workshop on qualification of novel methodologies held in April 2023
- EMA to develop an action plan on the basis of the workshop report, and consult the sounding board

Cooperation at the HTA/regulatory interface

To facilitate evidence generation planning developers will be able to apply for parallel EMA/HTA body (HTAb) scientific advice from September 2023, when EUnetHTA 21 ceases to operate, until January 2025, when Regulation (EU) 2021/2282 on Health Technology Assessment will become applicable. G-BA will function as the HTA coordination contact. The selection criteria will be identical to the ones of the HTA Regulation. The result of the selection will also depend on the resources available to each HTA body. A minimum of two HTA bodies will actively participate on a voluntary basis. If the minimum number of active HTA bodies is not reached, the request will continue as EMA-only scientific advice. As an outcome of the procedure, developers will receive a scientific advice letter from EMA and individual written recommendations from participating HTA bodies.

FOLLOW-UP:

- EMA together with G-BA (for participating HTA bodies) to monitor the uptake and experience with the transitional arrangements for the Parallel Consultation until arrangements under the HTA Regulation come into operation

Progress with the implementation of initiatives to optimise the application of the PIP framework

The background leading to development of the stepwise paediatric investigation plan (sPIP) pilot was presented and the experience so far following the launch of the pilot in February 2023. So far 12 enquiries relating to the pilot were received and the first two sPIP applications have been received. The medicines are to treat diseases mainly in the metabolic and neurology therapeutic areas and the majority were at very early stages in the process. The main reasons sponsors were interested in the sPIP pilot were due to uncertainties related to early development and challenges with aspects of clinical development in ultra-rare conditions such as dose finding or endpoints.

EMA outlined the main changes in sections B-F of the revised scientific document for which a draft was already presented to stakeholders earlier in 2023. The revised document, which is the basis for the PDCO Summary Report, has been simplified and updated to reflect latest approaches to paediatric development including assessment experience. Before publication the document will be sent for a final round of consultation before September 2023. From the moment of publication, the use of the revised document is optional in new submission for a 6-month period; afterwards it becomes mandatory. Applicants are encouraged to use the voluntary submission period and provide feedback.

FOLLOW-UP:

- Trade associations to cascade information about the new sPIP framework as well as the changes to the Key Elements form and the Summary Report template, to ensure uptake by developers
- Review of experience from the sPIP pilot, once completed, and provision of recommendations for further strengthening of the concept

- Provision of user feedback on the new Key Elements form and Summary Report template, facilitated through the sounding board

Development of complex generics

Industry highlighted as challenges the lack of a clear definition of complex generics, different regulatory pathways, and the difference between generics/hybrids with implications for subsequent phases of product lifecycle. A call was launched for establishing a decision tree or a flow chart to help companies develop their products, clarification whether equivalence studies are required or a biowaiver can be granted, as well as defined scenario for acceptance of data when non-EU comparator product has been used.

EMA recognised the increasing use of the term 'complex generics' to reflect the nature of the products themselves even without a formal EU definition. In general, the guidance on bioequivalence is applicable; the hybrid route allows flexibility (bridge v's formal bioequivalence). Product-specific bioequivalence guidelines are considered, where relevant. There is an opportunity to discuss tailored approaches through scientific advice including pilot parallel scientific advice with FDA for complex generics.

FOLLOW-UP:

- EMA to review the presentation of information on the EMA website of relevance to complex generics, e.g. links to specific guidance and papers, and consider a Q&A on views regarding complex generics

Report from the Focus group on provision of scientific advice for medicinal product developments comprising of drug-device combinations and drug-companion diagnostic combinations

Industry presented the results of the Focus group analysis of study cases illustrating scientific questions on medicinal product development in combination with medical devices or companion diagnostics and stakeholders that are relevant for multi-stakeholder discussions. Industry welcomed the broad stakeholder focus group work conducted so far and expressed the need for a joint discussion platform with EMA, SAWP, NCAs, NBs and pharmaceutical industry to discuss questions on (co-)development strategy for medicinal product developments comprising of drug-device combinations (DDC) and drug-companion diagnostic (CDx) combinations.

Notified bodies explained the background where even before the introduction of the MDR and IVDR, they were not allowed to provide any kind of advice or pre-certification activities that could be perceived as "consultancy". There are ongoing discussions on EU level on how notified bodies could provide "structured dialogue" which should be understood as (sometimes also pre-submission) exchange of technical information and regulatory guidance between the notified body and the manufacturer towards clarification of regulatory requirements (i.e., "what needs to be fulfilled") but precludes assisting manufacturers in finding solutions to fulfil such requirements (i.e., "how to comply"). Engagement of a notified body in the scientific advice process is currently not possible. Currently, scientific advice for devices can be given by expert panels on some high-risk medical

devices, and in some case by the EU Reference Labs for IVDs and by some Member States competent authorities.

Experience was shared by a national competent authority representative in terms of operating in the medicinal product/medical device interface. Interaction possibilities of different decision-makers were presented and challenges for NCA clinical trial assessors pertaining to different medicine/device combinations were discussed. Common challenges included the use of different language/terminology between medicines, medical devices and IVDs; the different timelines for clinical trial and clinical investigation/performance study approval; requirements of the combined product often using an investigational device/IVD; and the need to incorporate medical device/IVD expertise in the clinical trial application assessment. In terms of improvement proposals, a better understanding of development issues across medicines and devices is needed, starting with familiarisation with different terminologies, progressing with understanding regulatory requirements across fields, collaborating in the assessment and leading to filling guidance needs and to collaborative interface guidance development.

Against the background of these exchanges and the discussion, also considering the current regulatory framework, it was agreed to continue work with a range of specific follow-up activities.

FOLLOW-UP:

- Focus Group to hold a debriefing from the platform discussion focusing on the proposed range of follow up activities and identifying opportunities for concrete contributions
- Members of the Focus Groups to document the outcome of the previous discussions in terms of scientific questions for scientific dialogue and expertise needs through a scientific publication for further dissemination to a wider audience
- Building on the existing pilot for advice by expert panels on high-risk MDs, developers are invited to explore the possibility to include high-risk MDs used in combination with a MP and EMA to build an operational bridge between expert panel (MD focus) and SAWP (MP focus), and later review the experience
- EMA to look into the possibilities of involving NCAs with device competence in EMA scientific advice on development proposals
- EMA to look into the options and specific actions related to developments in combination with medical devices including companion diagnostics within ACT EU