



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 September 2022
EMA/644334/2021

Highlight report from the 8th Industry stakeholder platform on research and development support

11 July 2022

Role	Name
Chair:	Michael Berntgen
Present:	<p>Industry: AESGP Christelle Anquez-Traxler, Klavdija Kmetec Alliance for Regenerative Medicine Jacquelyn Awigena-Cook, Stuart Beattie, Simone Biel, Mimi Choon-Quinones, Sibylle Herzer, Sarah Higham, Fiona Murray EFPIA Gesine Bejeuhr, Susan Bhatti, Tim Chesworth, Sini Eskola, Ansgar Hebborn, Inka Heikkinen, Claire Hill-Venning, Christine Mayer-Nicolai, Isabelle Stoeckert EUCOPE Alison Bond, Lucia D'Apote, Joao Duarte, Johanna Grames, Lars Hyveled-Nielsen, Niina Lantelankallio, Nadège Le Roux, Maren v Fritschen EuropaBio Seán Byrne, Bettina Doepner, Pedro Franco, Esteban Herrero-Martinez, Laura Liebers, Monica Mihedji, Marcello Milano Europharm SMC Parminder Kaur, Paula Sanchez Medicines for Europe Susana Almeida, Marta Baldrighi, Anne-Cecile Bayne, Sandra Cubas, Caroline Kleinjan, Juliette Omtzigt, Pavel Sebek, Beata Stepniewska, Nivedita Valentine MPP Stephan Affolter, Fanny Barbotin, Andreas Emmendoerffer, Shayesteh Fürst-Ladani, Jesus Rueda, Mike Wallenstein, Stefan Wehner Vaccines Europe Stephane Callewaert, Anna Czwarno, Anne Griffiths, Susanne Heiland-Kunath, Béatrice Huret, Solange Rohou</p> <p>EMA: Ralph Bax, Nathalie Bere, Michael Berntgen, Christelle Bouygues, Corinne De Vries, Gunter Egger, Falk Ehmann, Juan Garcia, Iordanis Gravanis, Peter Karolyi, Kristina Larsson, Thorsten Olski, Chrissi Pallidis, Marie-Helene Pinheiro, Stefano Ponzano, Stefanie Prilla, Sonia Ribeiro, Ana Trullas Jimeno, Ciska Verbaanderd, Thorsten Vetter</p> <p>EMA scientific committees and working parties, European medicines regulatory network: Paolo Foggi, Sabine Scherer, Martina Schüßler-Lenz, Bruno Sepodes, Violeta Stoyanova-Beninska, Maria Elisabeth Kalland, Jörg Engelbergs, Hilke Zander</p> <p>European Commission: Valentina Barbuto, Marco Capellino, Sara Rafael Almeida</p> <p>HTA bodies: Antje Behring, Chantal Guilhaume, Anne Willemsen</p> <p>Notified Bodies: Marta Carnielli</p>

This was the eighth 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

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



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 has been made on these items, and all were subject to follow-up discussions at the 8th meeting.

Strengthening the ecosystem of engagement platforms for evidence planning

A. Status update in terms of scientific advice capacity and development of proposals moving forward

As a follow-up to the discussion in November 2021 (see [7th Industry Stakeholder Platform on R&D support 23.11.21 - highlight report](#)), EMA presented the current status of scientific advice capacity. Significant progress has been made as the number of scientific advice requests requiring a delay in the start of the assessment is in the single digits since the July 2022 SAWP plenary meeting. This is due to measures taken but also due to the normalisation of the number of incoming requests.

The EMA further provided an update on upcoming and planned changes to the scientific advice framework. An update of the public guidance intended primarily to clarify the scope of scientific advice and which questions are not suitable for scientific advice as well as an update of the scientific advice briefing document template to facilitate the generation of subsequent assessment reports will be published in the coming months. Industry has been consulted in the process of these updates and will be consulted again before publication.

In the medium term, some changes to the SAWP composition to slight increase assessment capacity will be implemented in March 2023.

In the longer term, a number of initiatives and planned actions will affect scientific advice directly or indirectly; harmonisation of scientific advice on clinical trial design and clinical trial approval will be pursued via the Accelerating Clinical Trials in the EU (ACT-EU) priority action 7 (PA7); EMA stewardship through regulatory interactions and scientific advice agility will be pursued via the follow-up actions of the PRIME 5-year report; patient involvement in activities relating to scientific advice (engagement, patient-reported outcomes, patient preferences) is taken up in various initiatives and a workshop is planned (see agenda item "Strengthening patient-centric development"); work is progressing on Joint Scientific Consultations with HTA bodies and discussions are commencing on scientific advice for medical devices; the EMA is developing tools to allow the EU regulatory network to tap into the EMA scientific advice repository; Q&As translating advice into public guidance in an expedited fashion is expected to commence in the oncology area, facilitated by the new working party structure.

Industry reiterated their availability to engage in discussions with the EU regulatory network and support activities in any way possible as well as the need to integrate the above and other ongoing or planned development support activities into a holistic transformation map to ensure coherence between them and that none are overlooked.

FOLLOW-UP:

- EMA to publish the revised public guidance clarifying scope of scientific advice as well as the updated Briefing Document template, following consultation with the sounding board

- EMA to present a more holistic transformation map of the development support framework at the next platform meeting

B. Progress report from the Focus group on review and strengthening the framework for qualification of novel methodologies

Industry presented the progress of the Focus Group work, outlining the 2 workstreams (Horizon scanning for future methodologies for qualification of novel methodologies [QoNM] as well as Procedural and expertise needs and options for outputs) and 4 case studies. The latter are planned to provide focus points for discussion: (a) Ways to improve communication and procedural flow between stakeholders (DEEP platform as an example), b) Biomarkers, c) Modelling & Simulation for BE studies and d) RWE – Qualification of data sources.

Focus Group discussions are progressing well with a timetable agreed by its members targeting a substantive report back to the Stakeholder Platform in December.

EMA announced that on the basis of the Focus group work a public multi-stakeholder workshop on the Qualification of Novel Methodologies platform is planned for the beginning of 2023. This will be complementary to a planned industry-led multi-stakeholder workshop on enhancing patient-centric outcome measures and clinical trials with Digital Health Technologies.

FOLLOW-UP:

- Recipients of the industry survey to contribute to the ongoing horizon scanning on the qualification of novel methodologies for medicine development (deadline 31.07.2022)
- Focus group to continue work acc. to their schedule and provide a final report at the next R&D platform in 4Q22
- EMA to progress the planning of a workshop on qualification of novel methodologies

C. First exchange on the opportunities to synergise EMA scientific advice on drug-device combinations and the Medical Device Expert Panels - Expectations from developer's perspective

Industry presented their views and expectations regarding the need for an "Integrated pathway" with reference to the EU medicines network strategy and in follow-up of the 5th EMA industry stakeholder platform on R&D support. Initial reflections on mandate and scope for the Medical device expert panels, the involvement of Notified Bodies as well as next step in the collaboration were presented, with a view to progress a pilot of multi-stakeholder scientific advice for medicinal products used in combination with medical devices.

EMA complemented these reflections stating that "Integrated pathways" is a comprehensive ambition with a number of players and is a mid/long-term perspective. The concept goes across the lifecycle of products and has a digital transformation component to connect relevant parties with state-of-the-art technologies. At this point EMA is focusing as priority on MDR/IVDR implementation as well as the operations of the expert panels; subsequently the development of the "Integrated pathway" concept will be progressed. Guidance on evidence generation (aka scientific advice) covering medicinal product and medical device / IVD is one element and the first step will be to clarify remits and ensure capacity. In this context the engagement with the expert panels requires clarification who can be the requestor and what type of technologies are in scope; this is different for MDs and IVDs. It would therefore be important to hear from developers concretely what type of remit they see for SA involving expert

panels, and which types of questions would benefit such SA. This information could support shaping a pilot, which ideally should focus on product/device combinations.

FOLLOW-UP:

- Industry (incl. MedTech industry) to provide an in-depth analysis of scope/remit for SA involving expert panels as well as typical types of questions that would be subject to such advice
- EMA to review such analysis and hold a follow-up call with industry participants, with a view to shape a pilot for such advice
- EMA to consider future engagement opportunities on the refinement of the integrated pathways concept

D. Progress with the repurposing pilot – interim feedback

EMA gave an update on the progress of the repurposing pilot. It was indicated that the call for repurposing candidates was closed in February 2022 and that 35 applications have been submitted indicating a high interest. Some first insights on number of submitted projects, concerned therapeutic areas and champion status were shared. The screening phase of the candidate projects has recently been completed and EMA will shortly communicate to the champions the outcome of the selection of the projects to continue to scientific advice, including those that benefit of the provision of scientific advice free of charge in the context of the repurposing pilot.

E. Experience with the ITF framework for 3Rs and new approach methodologies (NAMs)

EMA highlighted its commitment towards the 3Rs principles (replacement, reduction, refinement) and gave an overview of the new 3Rs ITF initiative to provide support to the regulatory acceptance of so-called new approach methodologies (NAM) with the aim to increase the predictivity of non-clinical studies and gradually replace the use of animals in the testing of medicines. NAMs include, for example, in silico modelling and novel in vitro assays such as microphysiological systems (MPS), organ-on-chips and organoids. The objective is to encourage the development of NAMs, and to enable their integration in the development and evaluation of medicines.

In line with the reactivation of the CHMP/CVMP joint 3Rs working party in Q3/4 2022 the Agency invites industry and other stakeholder to share their experience and new 3Rs developments via EMA's ITF as well Scientific Advice. Industry welcomed the initiatives and committed to share relevant developments with EMA to inform the regulatory network and enable the 3R activities to progress in line with EMA's strategies.

Continuous improvement and strengthening of paediatric procedures

A. Progress report from the Focus group on the practical application of principles relevant for the PIP framework

The objective of this group is to develop further the principles that were established in the Focus group on the concept of an 'evolutionary' PIP (e-PIP) in order to guide the practical application. The primary focus is on the 'evolutionary' PIP to support the preparation for piloting and testing of the concept. Furthermore, the initial discussion on key elements (KE) for a PIP in general should be matured to support a review of the applicable guidance.

An overview of the progress was presented. The group has discussed the e-PIP principles and on the KEs started with clinical studies: distinguished required clinical KEs from not required clinical KEs; merged some elements (e.g. study design features and study population, endpoints) and deleted some; focused required KEs text where appropriate. The group has also started discussions on the other studies included in PIP opinions (quality, non-clinical, modelling and simulation) with a view to apply these principles also to these studies.

The next steps in terms of the KEs concerns the finalisation of merged Opinion / Key element form. The aim is to implement the updated opinion form with revised KEs end of 2022 / early 2023.

Regarding the e-PIP, a first draft Guidance document is planned to be produced by the Focus group by September for further discussion. A pre-pilot should help with drafting the guideline and explore how the e-PIP can work in practice, using the current PIP application and evaluation framework.

FOLLOW-UP:

- Focus group to continue work acc. to their schedule and provide a final report at the next R&D platform in 4Q22

B. Response to the proposal for modifying the compliance check procedure

EMA provided an update on the PIP compliance check procedure taking into account work stemming from the EMA-EC Paediatric Action Plan where simplification and streamlining of administrative procedures is one of the main objectives, as well as feedback received from industry stakeholders including their concrete proposals for changes to the PIP compliance check procedure.

The average duration of compliance check procedures is systematically and significantly shorter than the 60-days legal timeframe (currently 30 days). Documentation requirements have been simplified, timelines are applied flexibly and partial checks not requiring scientific discussions are concluded by the Agency without PDCO involvement, saving significant time.

The industry suggestion to check compliance only when all PIP measures are completed appears not supported by the legal framework. The aim of the Paediatric Regulation is to ensure that evidence submitted to support a regulatory application is generated in compliance with a PIP and makes it a condition for the successful validation of that application. It follows that any study report that is part of the submission dossier needs to be checked before confirming validity and verified whether compliant with the PIP. There is no restriction and no exemption for initial applications before the full completion of the PIP.

Similarly, there is no possibility to avoid suspending MAA validations in case a compliance check is missing as there is no margin of discretion in suspending or invalidating applications that do not comply with the requirements of the Paediatric Regulation. Experience shows however that such suspensions are extremely rarely as the majority of applicants submit upfront their request for compliance check.

Industry raised the need to avoid duplicate checks performed by EMA/PDCO and CHMP. EMA clarified that the different procedures have different purposes: compliance check is to determine that the evidence generated by a certain study is the same evidence as the one the PDCO requested in the PIP; validation is to verify that the documents are available in the submission and that they have been confirmed compliant; and assessment, performed by CHMP, is to establish the recommendation to grant or to refuse a Marketing Authorisation on scientific grounds. Therefore, there is no overlap and no duplication.

Last, the suggestion that compliance checks should be performed based on “essential” compliance with the key binding elements in the PIP decision and based on the compliance report referencing study result summaries or data in the regulatory application dossier, is acknowledged and already implemented in current practice.

EMA confirmed its commitment to further optimising processes on paediatric activities and future updates will be provided, as appropriate.

Strengthening patient-centric development

EMA presented the agenda for the ‘Multi-stakeholder Workshop on Patient Experience Data in medicines development and regulatory decision-making’ to be held on 21 September ([Agenda - Multi-stakeholder workshop Patient experience data in medicines development and regulatory decision-making](#)). The workshop includes presentations and invited participants from industry, including those within the current group. The workshop recording and presentations will be published on EMA website afterwards.

Industry highlighted their support for the workshop. They also presented an overview of EMA’s Qualification Opinion on IMI PREFER (framework how and when it is best to perform and include patient preferences in decision making during the medical product life cycle; [Qualification opinion](#)).

Collaboration at the regulatory/HTA interface

A. Progressing parallel Joint Scientific Consultations – experience from the first call and preparation of the second one

EMA and EUnetHTA21 provided an update on the status of parallel Joint Scientific Consultations (JSC) provided by regulators and HTA bodies. The developments since the start of the collaboration were revisited including the latest improvements to the process and mutual understanding. An overview was given how the current work on parallel JSC is embedded in the larger context of collaboration between EUnetHTA 21 and EMA, as reflected in the adopted joint work plan. It was briefly discussed how the experience informs the preparation of the application of the HTA Regulation.

Challenges were identified how to constructively progress discussions on evidence planning in the time between the conclusion of the current framework of parallel Joint Scientific Consultations and the date of applicability of the new HTA Regulation in January 2025. During the discussion stakeholders highlighted the need to address the levels of interaction during the JSC procedure between regulators and HTA bodies as well as the motivation to find options for discussion on evidence planning before the HTA Regulation becomes applicable.

FOLLOW-UP:

- EMA and EUnetHTA21 to continue updating guidance for parallel Joint Scientific Consultation based on experience, and as basis for future process under the HTA Regulation
- EMA and HTA counterparts to consider options for discussion on evidence planning involving regulators and HTAs after EUnetHTA21 and before the new arrangements under the HTA Regulation become applicable

B. Opportunities for strengthening information exchange to facilitate sequential decision making (CHMP Opinion and Joint Clinical Assessment)

Focusing on the interface between regulatory assessment and relative effectiveness assessment, industry presented initial reflections on information exchange to facilitate such sequential decision making. Starting points were the arrangements developed under Joint Action 3, as also described in the white paper "Future Model of HTA Cooperation", leading to questions what to exchange, when and by whom, plus the expected impact. Key elements from industry are the need to respect respective remits of EMA and EUnetHTA21/EU-HTA-CG, transparency towards the developer with regard to in any product-specific information exchange between EMA and EUnetHTA21/EU-HTA-CG and ensuring confidentiality. EMA and EUnetHTA21 noted this initial feedback. They are currently working on arrangements, which can be tested with joint clinical assessments under the current work plan. Industry were invited to bring forward live assets to further develop such arrangements, which will inform practices under the HTA Regulation.

FOLLOW-UP:

- EMA and EUnetHTA21 to continue defining processes also considering the feedback on clarity of scope and roles and responsibilities, for a discussion at a future platform meeting

Follow-up from the 5-year report on the experience with the PRIME scheme

In follow-up to the discussion at the 7th Industry stakeholder platform on research and development support in November 2021, 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. Consultation of relevant Committees, Scientific advice working party and governance bodies are ongoing regarding the time point for access to the scheme, opportunities for greater continuity and flexibility in the provision of regulatory/scientific advice to PRIME developments and the possibility to introduce a submission readiness meeting ahead of the marketing authorisation application (MAA) to review the status of key development aspects and the implementation of previous advices to facilitate accelerated assessment. EMA also informed of their plans to update relevant guidance by Q4 2022 and provide greater clarity on the rules of engagement and conditions for continuation of PRIME support throughout the development lifecycle. The efforts were generally welcome by Industry representatives including the possibility for additional engagement between the kick-off meeting and the MAA, as well as the plans to improve existing guidance provided any criteria defined for the level of engagement will not be overly restrictive.

EMA also highlighted that to optimise the support to PRIME products, it will be important to have greater transparency on applicants' plans for regulatory interaction. To this end, a roadmap of regulatory interactions is envisaged to help inform regulators, e.g. of upcoming scientific advice requests. In addition, the concept of the PRIME development tracker was presented. The tracker covers the most frequently encountered areas that were either the subject of scientific Advice or of Major Objections in the MAA, as per the PRIME 5-year analysis. The document is envisaged to be submitted by the company and updated at key regulatory interactions (SA) or ad-hoc, when needed. It would also be a blueprint for the PRIME kick-off meeting discussions, and a summary for the submission readiness meeting. The submitted document will be accessible to the rapporteur team and SAWP, to support a ready overview of the development status for upcoming regulatory interactions.

FOLLOW-UP:

- EMA to consult industry through the PRIME contacts on the key elements of the recommendations that directly affect their work, including the roadmap of regulatory interactions and development tracker, as well as the submission readiness meetings (timing, supportive documentation)

- EMA to update PRIME guidance and communication by 4Q22

Follow-up on the “Orphan Maintenance Assessment Report” survey

The EMA Survey on the Orphan Maintenance Assessment Report (OMAR) aimed at gathering information from various stakeholders on their current experience with OMARs. The survey was conducted from October to December 2021. The survey was disseminated to EU/EEA National Competent Authorities (human and veterinary), patients’ organisations, healthcare professionals, academia, health technology assessment bodies, payer community and pharmaceutical industry. 79 contributions were received.

The data has been analysed and discussions are ongoing with representatives of the Committee for Orphan Medicinal Products (COMP) towards a continuous improvement of the OMAR publication process. Industry stakeholders were the main responders to the survey as well as users of the OMARs. The majority of the stakeholders find the overall information contained in the OMAR informative and they are used for a variety of purposes, both at designation and maintenance stage. Several suggestions were collected through the survey and included e.g.:

- improve the visibility and search function of OMARs on EMA website;
- advertise the possibility of a pre-assessment meeting on EMA website;
- administrative suggestions (e.g. include Approval Commission Decision date, share full list of literature reference, maintenance of orphan criteria presented in tabular form);
- improve dissemination to some stakeholder groups (i.e. patient organisations);
- ensure same level of details across OMARs and provide more detailed information throughout the report.

Progress with the implementation of the Companion diagnostics framework

In follow-up to the discussion at the 6th Industry stakeholder platform on research and development support in June 2021, EMA provided an update on the implementation of the Companion Diagnostic (CDx) framework. EMA highlighted the complex EU regulatory environment for CDx and their corresponding medicinal product(s), with a specific focus on the new requirements introduced by the EU In vitro Diagnostic Regulation (IVDR, Regulation (EU) 2017/746). Regarding the implementation of the CDx consultation procedure, EMA adopted and published in December 2021 draft guidance and procedural documents for public consultation. Following the end of the public consultation in February 2022, documents were revised taking into account feedback from external stakeholders. In June 2022, the final procedural guidance and associated documents were published on the EMA webpage [Medical devices | European Medicines Agency](#). In addition, EMA started accepting the first CDx consultations in January 2022. The presentation concluded by highlighting several topics that require further reflections such as the publication of the CHMP assessment report on the CDx consultation, information on CDx in the product information of the medicinal product, and more visibility on yearly estimates for expected CDx consultations.

Industry representatives shared learnings from their side based on the first experiences with the new CDx consultation procedure. Challenges related to timelines advocating for the possibility of clock-stop

in case needed, procedural aspects, communication flow, alignment between stakeholders, transparency and labelling requirements were discussed.

It was concluded that all parties are on a learning curve hence the need for close interactions between stakeholders to facilitate and optimize this process. EMA highlighted there should be a communication flow between the medicinal product applicant and the device manufacturer to keep each other reciprocally updated on their respective procedure (marketing authorisation application and certification) e.g. on timelines and requested data, as the EMA cannot disclose such confidential information to another party than the applicant.

FOLLOW-UP:

- EMA to initiate a review of the experience once a reasonable number of companion diagnostic consultation procedures have been processed, to facilitate mutual learning involving all players (incl. medical device industry as well as Notified body representatives)