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Public consultation on EMA Regulatory Science to 2025

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* Name

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Introduction

The purpose of this public consultation is to seek views from EMA's stakeholders, partners and the general public on EMA's proposed strategy on Regulatory Science to 2025 and whether it meets stakeholders' needs. By highlighting where stakeholders see the need as greatest, you have the opportunity to jointly shape a vision for regulatory science that will in turn feed into the wider EU network strategy in the period 2020-25.

The views being sought on the proposed strategy refer both to the extent and nature of the broader strategic goals and core recommendations. We also seek your views on whether the specific underlying actions proposed are the most appropriate to achieve these goals.

The questionnaire will remain open until June 30, 2019. In case of any queries, please contact: RegulatoryScience2025@ema.europa.eu.

Completing the questionnaire

This questionnaire should be completed once you have read the draft strategy document. The survey is divided into two areas: proposals for human regulatory science and proposals for veterinary regulatory science. You are invited to complete the section which is most relevant to your area of interest or both areas as you prefer.

We thank you for taking the time to provide your input; your responses will help to shape and prioritise our future actions in the field of regulatory science.

Data Protection

By participating in this survey, your submission will be assessed by EMA. EMA collects and stores your personal data for the purpose of this survey and, in the interest of transparency, your submission will be made publicly available.
For more information about the processing of personal data by EMA, please read the privacy statement.

Questionnaire

Question 1: What stakeholder, partner or group do you represent:

- ○ Individual member of the public
- ○ Patient or Consumer Organisation
- ○ Healthcare professional organisation
- ○ Learned society
- ○ Farming and animal owner organisation
- ○ Academic researcher
- ○ Healthcare professional
- ○ Veterinarian
- ○ European research infrastructure
- ○ Research funder
- ○ Other scientific organisation
- ○ EU Regulatory partner / EU Institution
- ○ Health technology assessment body
- ○ Payer
- ◉ Pharmaceutical industry
- ○ Non-EU regulator / Non-EU regulatory body
- ○ Other

* ***Please specify:***

between 1 and 1 choices

- [ ] Individual company
- [x] Trade association
- [ ] SME

Name of organisation (if applicable):

EUCOPE

Question 2: Which part of the proposed strategy document are you commenting upon:

- (•) Human
- ( ) Veterinary
- ( ) Both

Question 3 (human): What are your overall views about the strategy proposed in EMA's Regulatory Science to 2025?

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

Question 4 (human): Do you consider the strategic goals appropriate?

Strategic goal 1: Catalysing the integration of science and technology in medicines development (h)

- (•) Yes
- ( ) No

Strategic goal 2: Driving collaborative evidence generation – improving the scientific quality of evaluations (h)

- (•) Yes
- ( ) No

Strategic goal 3: Advancing patient-centred access to medicines in partnership with healthcare systems (h)

- (•) Yes
- ( ) No

Strategic goal 4: Addressing emerging health threats and availability/therapeutic challenges (h)

- (●) Yes
- ( ) No

Strategic goal 5: Enabling and leveraging research and innovation in regulatory science (h)

- (●) Yes
- ( ) No

Question 5 (human): Please identify the top three core recommendations (in order of importance) that you believe will deliver the most significant change in the regulatory system over the next five years and why.

First choice(h)

7. Diversify and integrate the provision of regulatory advice along the development continuum

1st choice (h): please comment on your choice, the underlying actions proposed and identify any additional actions you think might be needed to effect these changes.

Science and technology in drug development are currently changing at a fast pace. Based on horizon-scanning activities, it will be essential for the regulatory network to advise efficiently on how such science impacts evaluation standards and benefit-risk in a collaborative and timely manner.

EUCOPE strongly supports the Agency's intent to invest the necessary resources to strengthen and streamline the current scientific advisory platforms so that product-driven advice can address multiple development options effectively. The current number of regulatory platforms providing advice and the advice system along the product lifecycle has reached a historical unsustainable complexity due to previous incremental implementation of specific legislations (Orphan, Paediatric, ATMPs, Pharmacovigilance).

To avoid creating an additional complementary advice mechanism, a more flexible and integrated R&D product support mechanism is needed, providing agile rolling advice that effectively addresses the key challenges and development milestones (e.g. PIP submissions, orphan designation, eligibility to expedited pathways, the transition to patient access and HTA, etc.). It is highly recommended that the new system is leaner, more flexible and faster while maintaining the open communication, interaction, and alignment between the relevant stakeholders.

Systematic involvement of patients and other relevant stakeholders such as HTA bodies, payers, healthcare professionals and others is key to achieve access to innovative therapies Such involvement is particularly important for complex products such as nanomedicines which cannot be fully characterised, ATMPs, innovative small molecules, drug-device combinations and emerging technologies which include challenges related to evidence generation (e.g. post-licensing needs and use of emerging sources of evidence from non-traditional sources e.g. registries, RWE) – for these complex products, the manufacturers of the originators or the follow-on products may need to provide additional data, continuous advice is therefore extremely important. This applies also to rare diseases where one pivotal study should satisfy requirements from multiple EMA committees and hence coordination between the committees should be strengthened significantly for the industry to be able to develop rare disease medicines faster for patients in need.

Such model can benefit from previous dialogue in cross-stakeholders initiatives (e.g. R&D Stakeholder Platform discussions).

Second choice (h)

17. Reinforce patient relevance in evidence generation

2nd choice (h): please comment on your choice, the underlying actions proposed and identify any additional actions you think might be needed to effect these changes.

Due to advances in technology, patients are very aware of their disease and treatment options. For many diseases, treatment might not even be available. Patients, parents and/or caregivers in some instances, particularly in rare diseases, likely know more about their disease, symptoms and daily living than any other stakeholder. Therefore, the Agency's proposal to increase the involvement of these in the EMA scientific committees is very much welcomed and EUCOPE encourages the Agency to proactively involve patients more and more in the routine evaluation of medicines. Adding to that, patients data preferences, reported outcomes(PRO) and other types of patient input to drug development and evaluation are being increasingly used in several regulatory jurisdictions at different timepoints during the lifecycle (as illustrated by EUPATI scheme). A stronger collaboration on how such role is perceived and used for different aims in healthcare can not only advance regulatory science but will also ultimately contribute to better patient-centred drug development, access and care.

A good example of this is the development of PROs: their validation and use in the clinical trials enables to make the patients' input heard more effectively and broadly during the development and evaluation process, helping sponsors, regulators and other stakeholders like HTA bodies and payers to place efficacy and safety data in a patient-centred context that can support benefit-risk and effectiveness assessments. A coordinated approach to PROs across therapeutic areas and a proactive update by the EMA of specific clinical guidelines on these would be welcomed. The outcome of public-private projects such as IMI PREFER can pave the way to establish a best-practice approach to patient-preference studies. It is also proposed to enhance international collaboration with regulators in ongoing initiatives, notably with regulators that are pioneering several initiatives on patient-focused drug development such as the US FDA.

Third choice (h)

5. Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products

3rd choice (h): please comment on your choice, the underlying actions proposed and identify any additional actions you think might be needed to effect these changes.

Over the past years, the EMA has identified an increase of scientific advice requests and marketing authorization applications for drug-device combination (DDC) products. The DDC market is growing and will continue to do so with advances in medical technology paving the way towards safer and more efficient patient care.

Developments in science and technology for medical devices may advance more rapidly than for medicinal products alone, which has also been recognized by the EMA, recently. Products that combine medicinal products for human use and medical device are bridging the divide between the pharmaceutical and the medical device sector.

Therefore, an integrated evaluation pathway is essential to ensure timely access for patient to innovative treatments for often unmet medical needs, especially in the context of the need to integrate regulatory advice throughout the lifecycle (see our first choice). Concerns around the timely implementation of the Medical

Device Regulation 2017/745 have clearly shown the relevance of effective collaboration between Competent Authorities and Notified Bodies and the necessity of adequate capacities being allocated.
Industry highly appreciates the accountability taken by EMA expressed in stakeholder interactions, the dedicated Medical Device website and the publication of the Q&A on implementation of the Medical Device and In Vitro Diagnostic Medical Device Regulations and the draft Guideline on the Quality requirements for drug-device combinations.

Hence, many details, as well as business processes, need to be further developed urging for EMA prioritizing this topic in the Regulatory Science 2025 agenda in order to foster and support early patient access to these innovative treatment options.

With regard to borderline products, under the new regulation, substances are now addressed and recognized as medical devices (Rule 21) and further guidance is given how to classify them. The same applies to products incorporating nanomaterials (Rule 19). However, there is still a common interest of regulators and industry alike for clear and selective guidance to ensure a straightforward and harmonized approach for the registration of these products within the European Union.
With the new definition of In Vitro Diagnostics (IVDs), the move to a risk-based classification and the introduction of new rules for companion diagnostic (CDx) devices, the IVD Regulation has changed the framework entirely.

The Competent Authorities (EMA and NCA), the Notified Bodies and industry are faced with challenges, which can only be handled in collaboration. The EMA's prospective approach presented during the R&D stakeholder meetings is well received by all stakeholders. CDx are generally codeveloped with an innovative medicinal product and regarded as novel and complex technologies in the area of precision medicines. These innovative research programs and the legal obligations should be a priority for the EMA regarding the mission to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health in the EU.

As a final note, this theme is of particular importance in the context of digital health and EUCOPE encourages the EMA to ensure a strong collaboration with the medical device community and Notified Bodies to ensure aspects such as qualification of new digital methodologies for drug development are carried out with the best available expertise and in a holistic manner.

Question 6 (human): Are there any significant elements missing in this strategy. Please elaborate which ones (h)

Question 7 (human): The following is to allow more detailed feedback on prioritisation, which will also help shape the future application of resources. Your further input is

therefore highly appreciated. Please choose for each row the option which most closely reflects your opinion. For areas outside your interest or experience, please leave blank.

Should you wish to comment on any of the core recommendations (and their underlying actions) there is an option to do so.

Strategic goal 1: Catalysing the integration of science and technology in medicines development (h)

	Very important	Important	Moderately important	Less important	Not important
1. Support developments in precision medicine, biomarkers and 'omics'	○	○	○	○	○
2. Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments	○	◉	○	○	○
3. Promote and invest in the Priority Medicines scheme (PRIME)	○	◉	○	○	○
4. Facilitate the implementation of novel manufacturing technologies	○	◉	○	○	○
5. Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products	◉	○	○	○	○
6. Develop understanding of and regulatory response to nanotechnology and new materials' utilisation in pharmaceuticals	○	◉	○	○	○
7. Diversify and integrate the provision	◉	○	○	○	○

of regulatory advice along the development continuum					

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation** you are commenting on:

Recommendation # 2: The ongoing Agency's level commitment to promoting ATMP development in Europe is recognized and supported vis-a-vis the implementation of the joint EMA-EC action plan.

Recommendation # 3. PRIME is a scheme designed to accelerate patient access to medicines that hold the promise to address high unmet medical needs. The first marketing authorizations for products designated as eligible to PRIME were granted only in June 2018; hence it is essential to review the performance of the scheme after 3 and 5 years, to ensure that it delivers the expected impact on public health (i.e. faster priority medicines to market). Proposed action to 'Leverage collaboration with patients, healthcare professionals, academia and international partners' is seen as very important. In particular, enhanced transparency is desirable is the exchange of information between EMA, FDA and other international regulators in aligning PRIME eligibility decisions with similar schemes' determinations. We concur that involvement of HTAs and payers in PRIME is key to ensure that scientific advice takes into account the generation of data along the development lifecycle to satisfy the needs of downstream decision makers on reimbursement; thus securing patients' access. Equally, the systematic involvement of patients and healthcare professionals in the multi-stakeholder early dialogue is essential to prepare healthcare systems for innovative medicines. In terms of capacity building to ensure that all applicants would continue to see the benefit of using the scheme, it is suggested that a fast lane approach would be designed for PRIME products which would include: shorter timeline for eligibility and kick-off meeting, continuous access to EMA contact person, rolling opportunity to receive advice on product development, as well as a similar 2-pager system used by the US FDA that allows for a pre-screening of applications, supporting efficiency).

Recommendation # 4: As highlighted in the core recommendation 'Facilitate the implementation of novel manufacturing technologies', manufacturing of medicines is evolving to embrace new models such as continuous manufacturing. Dialogue between Industry and regulator on the technical adaptation of the current regulatory framework is ongoing at EMA and ICH level. A more flexible and continuous mechanism of advice is desired (see also point *7. Here below) which will allow specialised experts in the EU Network to deeper understand the end-to-end process and innovative multivariate analysis that guarantee the product quality.

Recommendation # 5: One of EUCOPE's Top Priorities see the answer to Question 5 – third choice.

Recommendation # 7: One of EUCOPE's Top Priorities see the answer to Question 5 – first choice.

Strategic goal 2: Driving collaborative evidence generation – improving the scientific quality of evaluations (h)

	Very important	Important	Moderately important	Less important	Not important
8. Leverage novel non-clinical models and 3Rs	○	○	○	○	○

9. Foster innovation in clinical trials	○	◉	○	○	○
10. Develop the regulatory framework for emerging digital clinical data generation	○	○	○	○	○
11. Expand benefit-risk assessment and communication	○	○	○	○	○
12. Invest in special populations initiatives	○	○	○	○	○
13. Optimise capabilities in modelling and simulation and extrapolation	○	○	○	○	○
14. Exploit digital technology and artificial intelligence in decision-making	○	○	○	○	○

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation you are commenting on**:

Recommendation # 9. Clinical trials that employ innovative approaches in design and statistical analysis are gaining attention globally for their ability to enhance the efficiency of clinical development. EUCOPE welcomes the Agency's recognition that innovation in clinical trials offers the opportunity to demonstrate the benefits of medicines that could not be shown by more conventional methods. We strongly support the proposed underlying actions and in particular the intention to critically assess the clinical value of new and emerging endpoints and their role in facilitating patients' access to new medicines. We encourage the Agency to develop a new strategic initiative on Complex Innovative Clinical Trial Designs (including adaptive design and master protocols). Such initiative, ideally involving relevant stakeholders (developers, patients, clinicians, regulators, HTAs and payers) would: facilitate use and acceptability of such innovative clinical trial approaches, increase the regulators experience by allowing submission of case studies via a dedicated pilot programme and address different concerns from Regulatory Authorities (EMA and NCAs), Ethics Committees, HTAs. International collaboration with the FDA on the same matter would be beneficial, especially since such initiative is also ongoing there.

Strategic goal 3: Advancing patient-centred access to medicines in partnership with healthcare systems (h)

	Very important	Important	Moderately important	Less important	Not important
15. Contribute to HTAs' preparedness and downstream decision-making for innovative medicines	○	○	○	○	○
16. Bridge from evaluation to access through collaboration with Payers	○	◉	○	○	○
17. Reinforce patient relevance in evidence generation	◉	○	○	○	○
18. Promote use of high-quality real world data (RWD) in decision-making	○	◉	○	○	○
19. Develop network competence and specialist collaborations to engage with big data	○	○	○	○	○
20. Deliver real-time electronic Product Information (ePI)	○	○	○	○	○
21. Promote the availability and uptake of biosimilars in healthcare systems	○	○	○	○	○
22. Further develop external communications to promote trust and confidence in the EU regulatory system	○	○	○	○	○

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation you are commenting on**:

Recommendation # 16. Even if innovative medicines covering unmet medical needs receive a marketing authorisation, difficulties in obtaining reimbursement can lead to delayed, inconsistent or no access for patients across the EU. Therefore, activities to collaborate with and bridge to HTAs and payers are very welcome to develop a dialogue platform, to enable ultimately a single evidence generation plan, particularly in areas of unmet medical need and rare diseases. Collaboration with and sharing of information from regulators with HTAs and payers should lead to bridging and mutual agreement and understanding of decision frameworks, especially in aspects related to horizon-scanning, parallel consultation, unmet medical need definitions and effectiveness assessments. The end goal should be that clinically relevant innovative medicines can seamlessly be evaluated on clinical aspects linked to effectiveness that support reimbursement decisions, particularly rare diseases and products licensed under exceptional circumstances.

Recommenation # 17: One of EUCOPE's Top Priorities see the answer to Question 5 – second choice.

Recommendation # 18: EUCOPE supports the EMA's recent initiatives to clarify the role of real-world evidence in regulatory decision-making, notably the reflection paper on registries' use for that aim, to which we provided comments. We acknowledge the engagement of the regulatory network in ensuring that decisions concerning the requirement for registries as post-authorisation requirements are aligned and consistent and we believe those actions will bear fruits for post-licensing evidence generation. EUCOPE would like to suggest that further work on the acceptability of such evidence is carried out, especially taking into account drug development in areas such as rare diseases and personalised medicine: aspects such as natural history studies and single-arm studies in diseases where patient numbers are low can hugely benefit from post-licensing evidence generation through registries and other observational methods. It is important that EMA provides adequate advice and supports regulatory science initiatives that increase the suitability of such evidence for regulatory decision-making. This is an area where international collaboration (e.g. with the FDA) can be of particular benefit, as well as cross-stakeholders collaboration with partners such as HTA bodies and practitioners.

Strategic goal 4: Addressing emerging health threats and availability/therapeutic challenges (h)

	Very important	Important	Moderately important	Less important	Not important
23. Implement EMA's health threats plan, ring-fence resources and refine preparedness approaches	○	○	○	○	○
24. Continue to support development of new antimicrobials and their alternatives	○	○	○	○	○

25. Promote global cooperation to anticipate and address supply challenges					
26. Support innovative approaches to the development and post-authorisation monitoring of vaccines					
27. Support the development and implementation of a repurposing framework					

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation you are commenting on**:

Strategic goal 5: Enabling and leveraging research and innovation in regulatory science (h)

	Very important	Important	Moderately important	Less important	Not important
28. Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science	○	○	○	○	○
29. Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions	○	○	○	○	○
30. Identify and enable access to the best expertise across Europe and internationally	○	○	○	○	○
31. Disseminate and share knowledge, expertise and innovation across the regulatory network and to its stakeholders	○	○	○	○	○

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation you are commenting on**:

Thank you very much for completing the survey. We value your opinion and encourage you to inform others who you know would be interested.

Useful links

EMA website: Public consultation page (https://www.ema.europa.eu/en/regulatory-science-strategy-2025)

Background Documents

EMA Regulatory Science to 2025.pdf

Contact

RegulatoryScience2025@ema.europa.eu