Public consultation on EMA Regulatory Science to 2025

> Fields marked with * are mandatory.

* Name

* Email

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

Name of organisation (if applicable):

European Public Health Alliance (EPHA)

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.

Overall, the market authorization process needs to be modernized to guarantee that meaningful innovation reaches patients. This will be achieved by raising the bar for approvals of new medicines, modifying the current processes and prioritizing public health needs.

Here are some suggestions as to how this could be accomplished:

- Increase transparency of the system (Scientific Advice, Randomised Clinical Trials-RCT protocols summary, data and anonymised individual patient data (IPD) made publicly available)
- Conduct an impact assessment of the regulatory activities especially schemes which increase uncertainty at the expense of safety such as Priority Medicines Scheme (PRIME) & the medicines approved via conditional marketing authorisation (CMA)
- EMA should have a Strategy and Planning team which looks at the philosophy of the organization and evaluates the Agency's procedural regulatory decisions such as new approval schemes and pathways. External, non-industry experts should be included in such a team any outcomes from the team's work should be discussed with the public and should be publicly available
- Guarantee that RCT data (incl. IPD) are available to the scientific community for re-analysis and use supporting further drug development
- Demand comparative RCT whenever possible. Confirmatory studies should be powered on patient relevant outcomes and answer clinically relevant questions (e.g. comparative evidence). Patients (but also clinicians and health care payers) need to feel confident that a new treatment works in comparison to alternative options (if any) and this should be part of the risk-benefit assessment
- Require that one of the 2 RCT for approval should be done by an independent party. The EMA can demand raw-data for re-analysis. The EMA should make use of its existing power to mandate two RCT
- Require superiority trials whenever possible rather than non-inferiority trials
- The EMA should perform statistical analysis in house on raw data while ensuring the independence and integrity of the process. Such analyses should be available to 3rd parties
- Registrational protocols should be made publicly available for comments before start of the studies (to avoid using suboptimal comparators)
- EMA should consider the duration of treatment in the assessment process
- EMA should enforce stricter criteria in post-marketing authorization trials and surveillance. This includes appropriate study designs and endpoints to close information gaps remaining at the point of marketing authorisation. This way, the Agency will be enabled to withdraw a market authorization in case of worrisome toxicity and safety findings during the post-marketing studies.

Furthermore, marketing authorisations could be challenged or adapted if post-authorisation data do not confirm assumed benefits on relevant outcomes or in patient groups not covered by the data submitted for marketing authorisation. Toxicity data should be collected during RWD.

- Demand better statistical analysis of observational data (incl. public registration of a detailed study protocol and analysis plan, before start of the study)

We welcome the linking of specific regulatory remarks to later HTA decisions. Of importance, regulatory requirements could be adapted, so they meet the demands of HTA payers and society. The pre-market phase of the development of a medicine provides for a unique opportunity to generate evidence for healthcare decision making. Experience shows that this sort of evidence is unlikely to be generated after marketing authorisation.

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)

9. Foster innovation in clinical trials

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.

The EMA should endorse a patient-centric approach as opposed to a drug-centric approach.

To this end, it is important to strengthen the scientific rigour and relevance of RCT's used in the marketing authorisation process. Large simple RCTs in the later phase of development should be supported to collect meaningful data on the patient groups that will be treated in clinical practice. Gender differences and other relevant subgroups (such as women, older people with co-morbidities, pregnant and breast-feeding women) must be reflected in RCT.

Independent data analysis and trial pre-registration (registered report) and independent input into the trial design (or at least the ability to comment – e.g. expanded transparent scientific advice) should be pursued.

To this end, it is important to strengthen the scientific rigour of RCT's used in the marketing authorisation process. RCTs should include a population that represents that to which the intervention is intended, including special populations, women and elderly. Data from studies used for authorisation should be available for re-analysis as is the case with the U.S. Food and Drugs Administration (FDA). Patients deserve better information on the medicines they take, this is why the Agency should demand better and more evidence from drug developers in the pre-market stage of drug development.

EMA should consider the duration of the treatment in the assessment process.

In order to improve trust in the EU regulatory system, it could be envisaged to a) demand comparative RCTs where possible, b) require that one of the 2 RCTs for approval be done by an independent party, c) pool resources across Member States to do meaningful-pragmatic RCTs responding to the right questions of clinical practice, d) require superiority trial whenever possible rather than non-inferiority trial,e) studies should be done to validate surrogate endpoints. Moreover, the use of surrogate endpoints should be discouraged nor accepted where final outcomes are achievable within a reasonable timeframe.

In terms of the post-marketing authorization generation of evidence (about the efficacy and safety of new medicinal products) emphasis should be paid to the reporting of adverse effects.

As far as so-called real-world data (RWD) is concerned, its use depends on the questions the regulator seeks to answer. It is therefore critical to reflect on the questions that can be answered by RWD before unconditionally endorsing RWD use in the regulatory decision-making, e.g. while RWD can be used to characterise the patient population in clinical practice or to collect data on resource use it is hardly possible to generate robust data on treatment effects unless these effects are very large.

It is thus the task of the EMA to clearly define the scope and questions, the regulator wishes to answer when using RWD. The regulator should view RWD as supportive evidence or signal eliciting evidence but should be cautious using this data to establish clinical effectiveness due to high confounding. Furthermore, there needs to be a distinction between Real-world data (RWD) and real-world evidence. RWD should include pragmatic trials as in "close to everyday practice". "Close to everyday practice" is independent of the study design, it can be done in uncontrolled (single arm) and controlled (both non-randomised or RCTs) trials.

In addition, appropriate quality criteria should be defined before any use of RWD (indicatively: who assesses the data, what is high-quality and to whom, is the appropriate infrastructure in place to collect and assess this sort of data, what are the checks and balances to protect against bias).

Second choice (h)

> 11. Expand benefit-risk assessment and communication

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.

> The push for accelerated approvals and the proliferation of conditional approvals must be evaluated against the original purpose of these flexibilities. They need to remain the exception as they increase uncertainty and put patient safety at risk. Hence, patients need to be fully aware of the harm-benefit ratio of these products. This must be clearly and sufficiently communicated to them (as well as to health care professionals and prescribers).
>
> The agency should ensure that submitted data answers clinically relevant questions rather than just demonstrates efficacy. Regulatory decisions should be guided by clearly defined, unmet public health needs.
>
> Pharmacovigilance activities should remain a priority for the Agency.The Agency should first and foremost guarantee that the medicines on the market are safe, and the activities of pharmacovigilance should be strengthened with drugs arriving on the market at an early development stage.

Third choice (h)

> 22. Further develop external communications to promote trust and confidence in the EU regulatory system

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.

> It is of utmost importance to maintain European citizens' faith in the work of the EMA. The Agency needs to welcome and endorse constructive criticism and foster a dialogue with critical voices. Most importantly, it needs to proactively dispel any mistrust caused by the links with the pharmaceutical industry. The EMA is a regulator defending the public interest and promoting public health In terms of the relationship with drug developers, the Agency must show they care for patients by 'punishing' the companies for not bringing relevant evidence, for not reporting post-authorisation studies on time. The EMA needs to make data publicly available and promptly recall the marketing authorisation when data is available. The perception of the Agency's independence and integrity are as important as the reality itself. Therefore, it is the Agency's responsibility to proactively dispel any fears about regulatory capture.
>
> The strategy of the EMA should include a reflection on the increasing risks of conflicts of interest raised by the planned strategy, which proposes to increase considerably scientific advice and early relations with drug developers, with the risk to transform the EMA into a co-developer of medicines. The set up of an ethics committee with external and independent personalities should be considered.

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

A critical review of the implementation of the orphan drugs legislation is important to ensure that the incentives foreseen by the legislator are not abused, misused or overused to the detriment of patients. The Strategic Reflection also lacks a critical reflection on the need for better quality clinical trials (e.g. randomisation).

Moreover, there is a need for strong recommendations to improve pharmacovigilance and monitoring of approved drugs. With the accelerated approval schemes and a shift of evidence generation towards post-approval, pharmacovigilance and monitoring of products on the market are even of higher importance.

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:

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**:

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**:

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