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# Public consultation on EMA Regulatory Science to 2025

Fields marked with * are mandatory.

* Name

* Email

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

***Name of organisation (if applicable):***

Mario Negri Institute for Pharmacological Research

### 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*.

The landscape of pharmaceutical research and development processes largely changed in the past decades and the attempt of the EMA to keep the pace is valuable. The EMA is the guarantor for the marketing authorisation of effective and safe drugs in the European Union, with the final aim to contribute to the well-being of the European Union citizens and correct functioning of national health systems. This should remain the primary perspective of the EMA; other interests, such as those related to the industry and national economies or scientific innovation, are only important as far as linked to tangible and meaningful benefits for patients and healthcare systems.

### 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

Comments on strategic goal 1 (h):

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

The current strategic reflection appears to give a nod to techno-driven pharmaceutical innovation rather than public health goals. While the implementation of new technologies and methods, such as the use of clinical routine data, big data, 'omics, artificial intelligence, may represent complementary tools to be used for decision-making, the licensing of drugs should still rely on relevant evidence generated by reliable clinical studies.
The Agency should primarily serve the needs of health professionals, patients, and citizens who must be reassured that the standard for drug regulation is high enough to guarantee that meaningful innovation reaches patients. The strategy foresees a role for regulatory agencies in "catalysing the translation of scientific and technological innovation into improved patient-centred healthcare". This makes extremely relevant a close relationship between the Agency and the manufacturers. While this may be appropriate in limited cases, for instance when very advanced therapies are under scrutiny, it may also affect the actual or perceived independence of the Agency.
To mitigate these risks, the Agency should ensure that its role in scientific advice does not influence the evaluation activities. Improved transparency of the system, in particular concerning the advice on clinical development, the bases for decision-making, and wider access to clinical data, including individual-participant data would serve to increase the Agency accountability and build trust in its independency. The business model of the EMA is also a matter of concern: about 90% of its budget derived from fees and charges in 2018. This poses conscious and unconscious pressure to the Agency to please the "costumers". The Agency should proactively dispel any concerns about regulatory capture.

### 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.

We fully endorse the need for a better alignment between the regulators' and HTA bodies/payers' needs, in terms of evidence suitable for their decision-making process. The EMA should base its decision on data that are reliable and applicable to the population and context of care. The main tool to achieve this goal is promoting randomised clinical trials designed to respond to questions relevant to regulators and downstream decision-makers.

For instance, the choice of the study population should closely reflect the group of people that will use the treatment under investigation, including the elderly and women if appropriate. Comparative studies are essential to understand the place in therapy of a new drug when therapeutic alternatives are available. The definition of the efficacy profile of a new treatment –that along with quality and safety constitutes the EMA mandate- intrinsically includes the definition of a benefit over the current standard of care, if available. More relevant outcome measures should be adopted in pivotal trials to ensure that the benefit-harm assessment of a new drug is based on clinically meaningful measures.
In summary, the EMA has the opportunity, e.g. through its regulatory guidelines, to push the methodology of pivotal randomised controlled trials toward a pragmatic approach. The Agency could request that one of the two randomised controlled trials for approval adopts a pragmatic design and, possibly, is conducted by an independent party.

## Second choice (h)

18. Promote use of high-quality real world data (RWD) in decision-making

## 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 use of data generated outside the context of a randomised trial is surely important to assess the value of a new drug fully. For instance, observational designs are informative in the pre-market to estimate the burden of a disease or post-marketing to study the long-term safety of a given treatment or explore the use of resources. Monitoring the effectiveness and safety of a new drug during the clinical routine is welcomed. Larger and more heterogeneous populations than those included in clinical trials are exposed and new drugs may be assessed in combinations or as part of therapeutic strategies. The EMA should be more pro-active in requesting or recommending post-marketing authorisation trials aimed to complete the evidence at the time of approval. Studies of active pharmacovigilance may be particularly needed as the safety profiles of new drugs is rarely established when a drug enters the market. The EMA website should clearly report which post-authorisation studies were committed to a given marketing authorisation holder for a drug and keep tracked the status of their conduction.

Regulators should not endorse the use of data collected during the clinical practice for regulatory decision-making unconditionally. Its use depends on the questions the regulator tries to answer. The advantages in terms of applicability and generalisability of data collected during the clinical practice have to be balanced with two main drawbacks. Firstly, the quality of these data, often collected for purposes that differ from that of research, is often suboptimal and may decrease the reliability of the evidence generated through them. Secondly, data generated in the clinical practice are usually analysed in the context of observational studies. A careful assessment of biases is of utmost importance and regulators should keep in mind that it is hardly possible to generate robust evidence on treatment effects unless these effects are very large. In addition, the same level of transparency achieved in the last years for clinical trials (registration, publication of the results, etc.) should be mandatory also for observational studies.

Third choice (h)

11. Expand benefit-risk assessment and communication

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.

We acknowledge that the EMA and other regulators need to tackle the inevitable tension between faster access to drugs for seriously debilitating diseases and the generation of a sufficiently large evidence base to support their benefit-harm assessment. Accelerated and conditional approvals may be powerful tools in a small subset of situations, but they should remain exceptions. The EMA should work with other stakeholders to better define the concept of unmet medical need. Post-marketing research is often unable to fill the gap of information at the time of approval, and the increased uncertainty may put patients at risk of being exposed to either a non-efficacious or a non-safe drug. In addition, the EMA should address the issue of communicating this uncertainty to health professionals and patients. When introduced onto the market, a drug is thought to be safe and effective and this often creates obstacles to post-marketing research.

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

We would suggest including an assessment of the implementation of the orphan drug legislation. It would be important to fairly evaluate its impact and highlight possible misuse of the incentives foreseen by the legislator for the development of drugs for rare disease. Given the so-called orphanisation of common disorders, especially in cancer due to the advancement in genomics, a revision of the definition of rare disease (or condition) is to be promoted.

**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