

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

Please specify: Press/media/NGO/Not-for profit organisation/other scientific organisations/policy maker, etc.

Not-for-profit organisation - medical journal - made up mainly of health professionals, committed to providing independent information on drugs and therapeutic and diagnostic strategies.

Name of organisation (if applicable):

Prescrire

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 strategy paper is merely a too much detailed list of all technical activities EMA would like to pursue rather than a strategic policy addressing patient needs. In our understanding EMA endeavours to be a co-developer and marketing enabler rather than a regulator and gatekeeper.

This paper widens considerably the legal mission of EMA: upstream in willing to manage fundamental research; downstream, in willing to circumvent HTA bodies and payers.

The proposed objectives/recommendations are mainly industry/science/technology driven with little focus on clear regulatory merits and responsibilities. There is a continuous trend towards early interactions, scientific advice, flexibilities and faster marketing authorisations with a shift from pre-marketing approval evidence-collection towards post-approval assessment. This implies that the burden of evidence-collection (including financing and responsibility) is shifted to other actors including hospital settings, health professionals, HTA bodies, payers, health authorities.

Before making use of new health technologies and observational data in the pre-approval regulatory process, they should undergo prior critical assessment to estimate if they are appropriate for this purpose.

The strategy is very unbalanced in giving very little emphasis on post-drug surveillance activities, such as pharmacovigilance. This word is mentioned only once in the paper, a clear indicator of what is missing in the strategy: a responsibility and an interest on what is going wrong with drugs.

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.

This strategic goal is primarily focused on means and tools to accelerated access of complex products to the market. Here EMA is going too far as a co-developer, a role that would dramatically weaken its core mission as regulator. By doing so, EMA gives the wrong signal to the pharmaceutical industry: focus research on lucrative therapies often coming on the market with little evidence of therapeutic progress and at continuously increasing price tags, making the minority of helpful drugs unaffordable and threatening the sustainability of health systems, even in high-income countries. Requesting reliable and robust evidence for an acceptable harm-benefit balance before marketing authorisation would be more appropriate.

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

Comments on strategic goal 5 (h):

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

We don't agree with this concept of regulatory science. Of course, EMA should develop its internal and external scientific capacity but only on its core mission, not in fundamental research. Improving evidence generation and scientific quality of evaluations are crucial.

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)

11. Expand benefit-risk assessment and communication

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.

EMA should require comparative randomised clinical trials versus standard therapy with patient-relevant outcome endpoints otherwise there can't be a question of patient preference.

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.

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.

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

Yes

- The strategy is not based on a needs-driven approach. What are the main public health needs to be addressed?
- The request for comparative trials versus standard therapy for marketing approval with relevant clinical endpoints on patient health outcomes.
- 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.
- There is a need for more post-marketing confirmatory studies with relevant clinical endpoints with proof of improved health outcomes. Better scrutiny and requirements of completion of post-marketing studies in

specified time limits.

- Better information and clarity of evidence of new treatments in respect to harms, benefits and uncertainties (with information on ongoing follow-up activities to address these uncertainties).
- Recommendations on improving the evidence generation unfortunately do not make suggestions for improving RCT designs, use of clinically relevant endpoints, or requesting comparative trials against standard therapy whenever this is possible (in line with Helsinki Declaration), inclusion of real target population (e.g. elderly people) and duration of treatment.
- Sometimes there is a lack of rationale behind the duration of new drug therapy in large pivotal randomized trials, and more specifically in adjuvant trials. The duration is often the result of a calculation by pharma on what would represent an optimal “return on investment” and exposes patients to unnecessary side effects and society to financial toxicity. We suggest that EMA – for instance when consulted for “scientific” purposes – also requires the investigation of a “shorter treatment duration arm”.
- Support for independent research and clinical trials.
- Improved transparency on scientific advice, clinical trial results and data.
- Support of drugs victims and activities to withdraw dangerous products from the market.

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’	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
2. Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Promote and invest in the Priority Medicines scheme (PRIME)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>

4. Facilitate the implementation of novel manufacturing technologies	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
5. Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Develop understanding of and regulatory response to nanotechnology and new materials' utilisation in pharmaceuticals	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Diversify and integrate the provision of regulatory advice along the development continuum	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>

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:

EMA has a clear role in the evaluation of ATMPs (2), medical devices (5) and nanotechnologies (6). In regards to precision medicines (1), EMA should not act as a co-developer and not support pharma companies to further develop “niche buster” models.

PRIME (3) expedited approval schemes are legitimate when there is a real unmet health need and small enterprises are at stake. The recommendations mainly focus on the promotion, identification of areas for increased investment, to speed further the pre-approval period and delay evidence gathering to the post-approval process. In our view, regulatory flexibilities should be applied only in fully justified circumstances and must ensure patient safety. Previous experience illustrates that shifting evidence gathering after market approval is problematic and exposes patients to harms.

Medical devices (5): EMA should proactively promote robust standards of clinical evaluation towards the European Commission and the Medical Devices Coordination Group (MDCG).

Scientific advice (7): it is high time to put an end to EMA's opaque and confidential practice of early scientific advice.

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	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. Foster innovation in clinical trials	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Develop the regulatory framework for emerging digital clinical data generation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
11. Expand benefit-risk assessment and communication	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. Invest in special populations initiatives	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. Optimise capabilities in modelling and simulation and extrapolation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
14. Exploit digital technology and artificial intelligence in decision-making	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>

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:**

Expand benefit-risk assessment and communication (11): in our view one main EMA mission is to grant marketing authorisation only to effective and safe medicines. Unfortunately, today too many new products get a marketing authorisation without robust data proving their efficacy/safety and comparative information against standard treatment. We invite EMA to consider its priority task is to improve the knowledge and transparency on data on the efficacy/safety profile including comparative information against standard treatments. Health professionals and patients need this information to make informed treatment choices.

Foster innovation in clinical trials (9): instead of what is proposed and weakening further existing
















mechanisms for marketing approval, we invite EMA to raise the bar with strong evidence requirements for marketing approval including comparative trials against standard of care treatment (whenever possible), using clinically relevant endpoints including quality of life and overall survival. Unfortunately, instead of requesting comparative trials and/or improving RCTs designs and meaningful endpoints that could lead to improved evidence generation in the pre-approval process EMA clearly gives preference to new unproven technologies and “big data”, artificial intelligence or surrogate endpoints whose utility still needs to be proven before being used at a large scale. Instead of improving evidence generation, we fear that the proposed recommendations will lead to even more uncertainties.

We agree with EMA’s mission described in the introduction: “The ultimate role of this network is to promote and protect the health of those it serves through medicines regulation. This means ensuring that both people and animals in Europe have timely access to medicines that are safe, effective and of suitable quality, as well as the information needed to use those medicines and make informed choices about their treatment.” In practice, today EMA does not help patients to “make informed choices about their treatment” because drugs come to the market based on very limited clinical evidence. With respect to article 168 of the TFEU, EMA should outline and promote solid evaluation standards based on a robust methodology, including for accelerate approval pathways or situations where comparative RCTs might not be appropriate. As a normal rule, the gold standard of genuine comparative randomised clinical trials would be a key element for “improving the scientific quality of evaluation” but is sadly absent of EMA’s strategy. We also call on EMA to design precise guidelines outlining these standards for particular evidence requested. The service “à la carte” through early scientific advice should be limited to exceptional situations.

With regards to special population initiatives (12), in particular pregnant women, we call on EMA to implement registries and to ensure that epidemiological studies are published without delays. EMA should also endeavor to set up a European centre on teratogenicity and fetotoxicity of medicinal products. Concerning treatments for elderly and/or multimorbidity patients, EMA should make sure that these categories are well represented in clinical trials.

The 2 last recommendations (modelling - 13, AI - 14) are potential risks for evaluation if they are used before being properly validated against relevant clinical endpoints. Observational data cannot replace an evaluation based on a rigorous methodology.

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:**

HTA, payers & patient relevance in evidence generation (15, 16, 17): Nowadays new authorised drugs are very expensive often without having demonstrated added therapeutic value compared to standard treatment. It is crucial that at the time of marketing approval, the necessary evidence and data are available to meet the needs of health professionals, patients, HTA bodies and payer organisations in order to provide informed decisions and guidance based on robust clinical data. While recognising the different and respective roles and tasks of regulators, HTA bodies and payers, regulators should better take into consideration their duty in requesting information and anticipate evidential standards needed to situate new authorised products in the existing healthcare systems. EMA should as well request data on (clinical) patient relevant endpoints like quality of life and overall survival.
















Big data (18): Instead of speculating on promises of big data and recommending the promotion of high-quality real-world data in decision making, EMA should on the contrary primarily engage in rigorous assessments of what is useful and feasible. EMA should also provide full assurance in respect to the General Data Protection Regulation (GDPR) and patients health data and scrutinise that data mitigation takes only place in the patients and public health interests. EMA should also make sure that artificial intelligence will not replace rigorous methodical evaluations. As a regulator, EMA has a duty to be more explicit and to explain concretely what they understand by concepts like “high quality real-world data”. We also advocate to replace the term “real-world-data” by “observational data”: data from RCTs are “real data” as well.

Electronic product information (20): we invite EMA to focus primarily on the improvement of the content of leaflets, to provide clear and accurate information for patients and health professionals to make informed choices, including alerts and pictograms mentioning specific safety warnings, for instance in case of

pregnancy. We do not share the suggestion of “personalisation of information according to patients’ needs” as this is not the objective of standardised approved product information. A personalised approach has to take place in a face-to-face discussion of the patient with a competent health professional.

Promotion of trust and confidence in the EU regulatory system (22): Trust relies on transparency and the independence of the EMA from commercial interests to fulfil its public health merits. To guarantee EMA’s independence and the aim of protecting public health rather than protecting industry interests, we strongly encourage EU authorities to pave the way for comprehensive public funding of EMA activities and functioning. We also invite EMA to further strengthen its conflicts of interest rules (including for external experts). Improvement of trust and confidence relies on transparency and access to information and data, for instance on pre-market assessments, pharmacovigilance, access to mock-ups in the EPARs, clinical study reports, guidelines on clinical research and on evidence requirements for marketing authorisations. Trust is gained by raising the bar for the provision of marketing authorisations to products with a favourable harm-benefit balance based on robust clinical evidence. For instance, in 2018 Prescrire assessed 30 new cancer drugs (or new indications). Only 11 were rated as an advantage and most with minimal benefit. According to Prescrire, over the time, EMA has clearly lowered the bar for drug evaluation. Sadly, nowadays, often marketing authorisation is provided on the basis of a single clinical trial, using laboratory or radiological endpoints that have not been proven to correlate with longer survival or better quality of life. The comparison is often inappropriate and non-blinded. Typical examples include elotuzumab (Prescrire Int n° 193) and ixazomib (Prescrire Int n° 194) in multiple myeloma, ofatumumab (Rev Prescrire n° 411) in chronic lymphocytic leukaemia, and alectinib (Rev Prescrire n° 415) and ceritinib (Rev Prescrire n° 416) in certain types of lung cancer. Prescrire also analysed in 2018 the evaluation data on three drugs authorised for multiple sclerosis: daclizumab, oral cladribine, and ocrelizumab. After analysing the initial evaluation of daclizumab and the serious and sometimes fatal harms already evident at this early stage, we concluded that it is more dangerous than useful (Prescrire Int n° 195). It is a typical example of a drug that should never have been authorised and in fact was subsequently withdrawn worldwide, but after much procrastination on the part of drug regulatory agencies and several patient deaths.

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	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
27. Support the development and implementation of a repurposing framework	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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:**

Shortages (25): all member states are faced with shortages of essential medicines; we consider that EMA has a clear role to address supply problems. Solutions should not be sought by lowering safety standards or GMP requirements. EMA might for instance set up a European network of voluntary pharmaceutical companies accepting to produce abandoned essential generic medicines. EMA might also set up a working group on Good Manufacturing Practice (GMP) of magistral formulations (for paediatric medicines or orphan drugs) and prepare a guideline to support health institutions in the production of such medicines in case of shortages. EMA should also encourage Member states and EU institutions to require pharmaceutical companies to make their authorised products available in Member states who claim them.

AMR (24): AMR is a dramatic example reflecting the pitfalls of a system which relies too much on the outputs of an industry-based model. Instead of looking again to new business models and new incentives, the international community should support independent public research infrastructures.

Vaccines (26): improved communication and complete transparency (including on ingredients, clinical trials) on safety and efficacy would contribute to improve trust.

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:**

Expertise (30): EMA is convinced that the best experts quite often might have conflicts of interest with the health industry and suggests a proportionate approach to potential conflicts of interest. We instead are convinced that EMA should require a rigorous conflicts of interest policy and work harder to identify independent experts. For its credibility and impartiality, EMA's staff and experts should be free of conflicts of interests with health technology companies. On many topics the provision of expertise on methodology, statistics are as important as the viewpoint of experts from the field.

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