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):

European Organisation for Research and Treatment of Cancer

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 regulatory science 2025 vision should be congratulated. It is important that the European regulator positions and clarifies its views. Regulatory science do evolve and changes have occured in many directions. It is not an easy matter. Datasets today are different, possibly more comprehenesive of multidirectional/dimensional data. Different type of datasets are developed and proposed to the regulators. It leaves the field with many questions as new agents enter the market. Several authors have confirmed that both in Europe and in the US a number of new agents do add limited clinical benefit to patients. Therefore true innovation is actually limited to few clinical situations. The commercial sector has proven to be desincentivized to perform research in the post- marketing phase. All this contributes to increase the gap efficacy-effectivenes and may not be patient centered. The 2025 vision may not have grasped fully these societal challenges. Moving from a European competence (authorisation) to a national comptence (access), a major EU gap, seems therefore to appear more as an observation rather than demonsttating how this is going to be tackled, possibly in a more balanced role of the commercial and non commercila sector. The importance of robust methodology through prospective clinical trials seems to be de -prioritized to the credit of observational data. collecting data is not new and serves hypothesis for research. Caution should be made on the fact that inherent bias to such data may be even more misleading than the potential artificial situation created by clinical trials. Though, it will be developed here in that pragmatic clinical trials in health care systems are possible. The perception that RCTs may not reflect reality is not linked to the randomisation but rather to the artifical and severe selectio criteria in commercial trials. The Agency should be instrumental in guiding the community for not compromising the robustness on which treatments are adopted.

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.

It remains unclear how closer collaboration between stakeholders as suggested, will actually be addressed, stimulated and solved. A major issue which needs to be addressed is the development , qualification and clinical validation of biomarkers and how they they will be evaluated by evolving technologies (assays). the bottlenecks have been clearly documented but the solution to catalyse such integration do not appear clearly. It appears that the predictivity of a biomarker is linked to the prevalence of a mutation and this varies accross tumor types. Therefore, trials which associate different tumor types represent undisputable progress for knowledge development, their regulatory validity should be subject to regulatory research. Manufacturing technologies would sound to be a later issue not really featuring in such strategic goal it would see, as an example.

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

○ Yes
◉ No

Comments on strategic goal 2 (h):

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

Though this section highlights key issues, it may miss providing evidence how the situation could be improved. It seems counterintuitive to stimulate early authorisation of borderline agents as it has been documented by several authors on relatively very early datasets and indicate that there is an intention to provide HTAs with better evidence of beneficial treatments, as actually benefice is unlikely to be demonstrated by small , immature dats sets, based on surrogate and possibly clinically irrelevant end-points. Challenges related to big data whether being used for diagnostics, treatment effect or simply monitoring may not be properly estimated as raising different types of challenges hence, solutions. A point which is particularly welcome, is the intention to involve academic research into evidence benefit-risks communication,. This should be further developped, notably in the direction that EMA should mandate independent trials, free of commercial interest to assess clinically relevant end-points among other important practical information to apply treatment in routine.

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

○ Yes
◉ No

Comments on strategic goal 3 (h):

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

RWD challenges may be under-estimated. Some aspects are even contradictory to the EMA guidance on registries pleading for disease rather than for product oriented RWD collection, when it seems here to be the case. While calling for PRO, the regulatory acceptance of HQQOL and PRO type of end-points remain unclear.EMA should stimulate level I evidence, robust conclusions as much as possible for demonstrating treatment effect based on clinically relevant end-points which impact on patient lives. Solutions impacting on patient lives should prevail over the simple recommendation of patient involvment in committtees. It is unclear how EMA wants to reconcile early access with some of the statements in 3.3.3.

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

○ Yes
◉ No

Comments on strategic goal 4 (h):

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

> It is unclear why re-purposing would differ than opimizing existing treatments, which may hit the clinic with limited information. Optimisation of treatments shodul not lead to multiple regualtory pathways. Solid evidence on how to use drugs in sequence, combination or duration should be subject to pragmatic trials , possibly in heath care systems. Doctors and patients need such type of information to address the gap efficacy -effectiveness. There is a value crisis in Europe, understanding and opimising their use after early market access datasets should be made possible . The systems should not to be different when it comes to using optimally or repurposing treatments for patients. We urge not to create too complex and varying regulatory pathways.

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.

> EMA should not re-create what is existing. Existing solutions should be consulted and used for fundamental and clinical research to bring more independence in the true evaluation of treatments. The concept of applied clinical research has been well communicated by organisation like EORTC, pleading for independent evaluation of the true value of treatment in pragmatic trials perforned in health care systems which would be optimal to inform access, based on which only appropriate long term monitoring of safety for instance can be envisaged based on RWD (refer to EORTC /EU parliament manifesto on optimizing treatments) . New regulatory science should re-synchronise and coordinate the role and expertise of different stakeholders in an re-engineeered process from discovery into access and care. This should include regulatory applicatio of specific designs (see comment above on mutitumor trials). Articles and concept principles are available upon needs.

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)

○ 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

○ 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

○ 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

○ 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

○ 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

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.

> As indicated, Europe would gain in a more balanced independent evaluation of treatments and specifically how to optimally use them in existing therapeutic strategies. Early access to breakthroughs in situations where there is no existing or poorly referenced treatments is not disputable. Observations indicate that the issue is not there but in the so many drugs which are costly and do not bring true therapeutic progress to patients. This can only be optimally achieved in an environment which is free of commercial interest.

Second choice (h)
○ 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
- ○ 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
- ○ 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
- ○ 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
- ○ 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

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 concept of RCT should be revisted. It is often opposed to RWD which is not a misleading comparison. Simple , robust RCT based on very limited eligibility criteria are best positionned to inform society. RCT is in fact understood as complex protocols, based on on long list of eligibility criteria, as usually done for commercial trials. If we would have randomized all patients amenable to immunotherapy for cancer in real life between long and short cours eof treatment, we would have now a robust evidence how long to treat patients with so expensive agents which may still generate long term toxicity, just an exmaple of a pragmatic independent RCT which should be mandated. Innovation in pragmatic, biology based clinical trials, longitudinally performed along side the the course of the diseases would be critical, for example, for addressing the next oncology challenges, patterns of resistance and relapse. As already indicated but important to repeat, research should be done on the understanding and role of trials designed to learn versus trials designed to conclude and how they should be respectively used in the process of development, approval and access. In addition, the role of observational data and how they can be articulated within the full span from discovery to care should be an impoartnt part of the EMA priorities

Third choice (h)

○ 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

○ 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

○ 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

○ 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

- ○ 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

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.

> The information provided in the comments throughout are self explanatory. The systems are heavily drug centered and not patient/clinic centered. In the era of precision medicine, systems should be re -engineered so that we move from the era where protocols were searching for patients meeting eligibility criteria to patients informed on the biology of their diease searching the appropriate protocol along side the evolution of their disease. There is no hint that such out of the box appraoch is being stimulated.

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

> The patient dimenssion is missing. It is being referred in the comments hereabove . A new agent is developped based on a picture of the disease a certain point in time. Many diseases have a history before and after which may not be relevant to a certain drug manufacturer while it is critical to understand the evolution of the disease. Therefore a vision would be to re-structure drug development around the patient and not around drugs. A longitidunal approach of disease need to be developed based on which development can happen. It requires to re-assess regulatory science which should involve other partners than the regulator and the manufacturer.

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	○	○	○	◉	○

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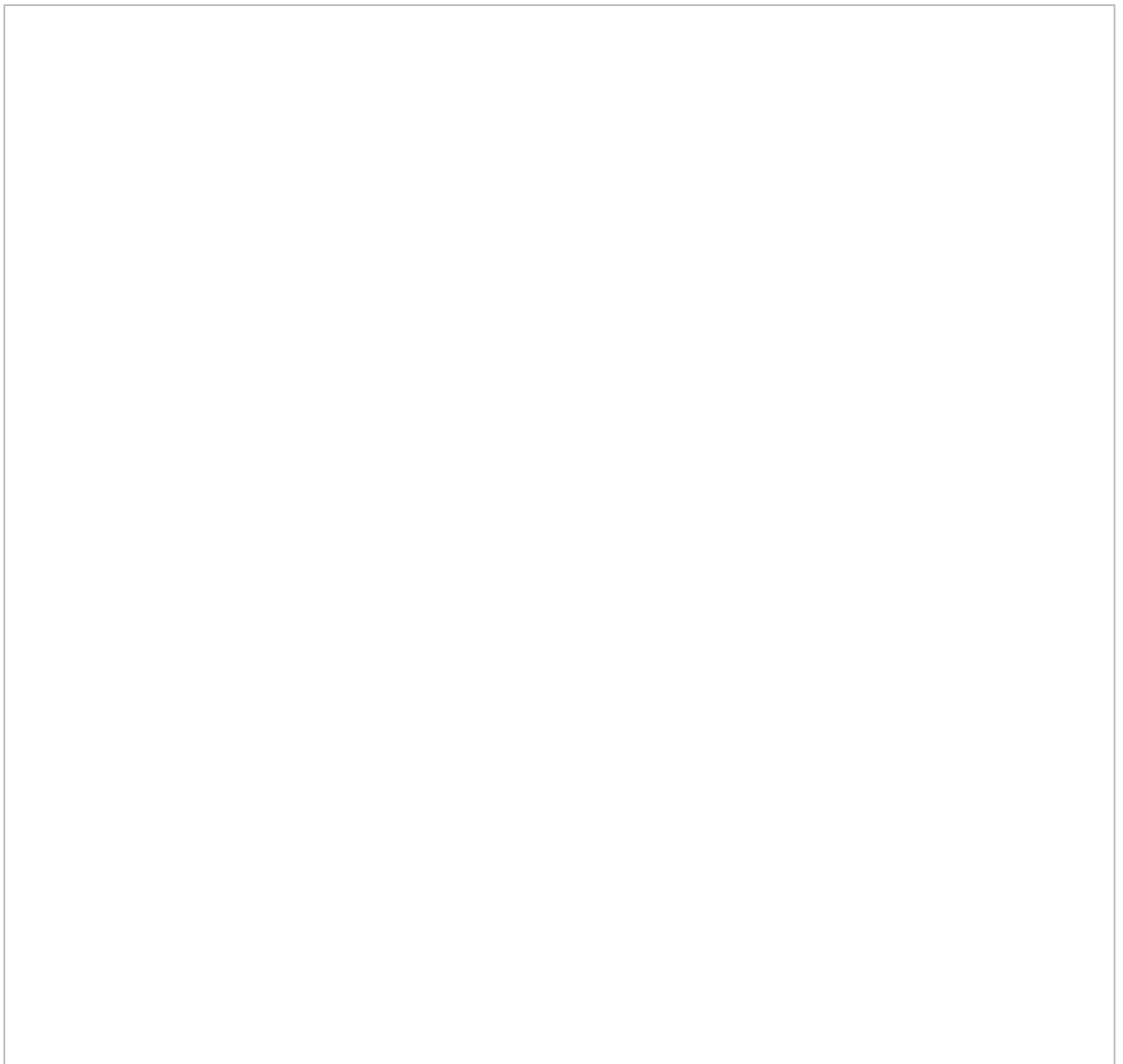
Thank you very much for completing the survey. We value your opinion and encourage you to inform others who you know would be interested.

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