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Public consultation on EMA Regulatory Science to 2025

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Introduction

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

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

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

Completing the questionnaire

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

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

Data Protection

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

Questionnaire

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

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

* ***Please specify:***

between 1 and 1 choices

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

Name of organisation (if applicable):

Vifor France SA (on behalf of the Vifor Pharma Group)

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.

Vifor welcomes the opportunity to participate in the public consultation. We believe that the strategy rightly places emphasis on supporting regulatory science and innovation to ensure patient access. As it is pointed out in the future regulatory science strategy, innovation has accelerated dramatically in recent years and regulators need to be ready to support the development of increasingly complex medicines.

We believe this is particularly true for nanomedicines, which have experienced enormous advances in recent years and can offer great potential for improving therapy in a range of different disease areas. Moreover, as an emerging technology, we also firmly believe that nanomedicines could be of strategic importance for European competitiveness and leadership in health policy making.

Nanomedicines are medicinal products that have at least one dimension in the nanoscale range (1nm to 100nm), which allows for preferential crossing of specific barriers within the body (e.g. cell membranes) to reach the drug target (e.g. enzymes). Nanomedicines exhibit phenomena and properties, attributable to their size and morphology, which are relevant to their safety, effectiveness and quality. Due to their unique physicochemical features, nanomedicines have the potential to offer treatment options for previously untreatable diseases. They cover a broad spectrum of therapeutic areas, affecting patients suffering from a variety of diseases, including multiple sclerosis, schizophrenia, cancer or anemia.

The complexity of nanomedicines raises questions of whether they can be considered for regulatory purposes in the same manner as other more conventional small molecule medicines. In particular, as an increasingly number of nanomedicines-based follow-on products are developed, this raises questions around how to demonstrate therapeutic equivalence to reference products.

We therefore welcome that the core recommendations include the effort to better understand the potential of nanotechnologies in human medicine. The actions proposed to achieve this do move in the right direction. In the following sections of this survey we further elaborate our thoughts on the regulatory challenges of nanomedicines.

In addition to the topic of nanomedicines we also believe that the following two issues require additional thoughts by the EMA in the next 5 years:

- Regulatory advice along the development continuum
- The use of high-quality real-world data (RWE) in decision making

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)

6. Develop understanding of and regulatory response to nanotechnology and new materials' utilisation in pharmaceuticals

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.

Vifor welcomes the EMA's intention to further develop the understanding of and regulatory response to nanotechnology and new materials' utilization in pharmaceuticals. We would like to specifically touch upon the issue of nanomedicines.

We believe that the current regulatory framework does not fully address the specificities and complexity of nanomedicines.

For the moment, the European regulatory network approves nanomedicines and follow-on products on an ad hoc basis. As it is not mandatory for nanomedicines and follow-on products to be approved via the centralised procedure at the EU level, it has been the case that NCA review has led to different approaches from one market to another.

There is a plethora of evidence showing that follow-on nanomedicines (e.g. intra venous iron-based nano-colloidal products) approved and available in the EU have different efficacy and safety profiles (Rottembourg et al., 2011; Agüera et al., 2015). Most of these products have been approved through a generic pathway under Decentralised or MRP procedures, which have proven inadequate in demonstrating their therapeutic equivalence to the originator products. The EMA has since developed guidance for some of these categories of products (e.g. Iron Sucrose Similars) however consistency in the treatment of nanosimilars by national regulators is still lacking – as explained in a recent paper by Klein K. et. al. on "The EU regulatory landscape of non-biological complex drugs" (Eur J Pharm Sci, 2019 May).

The establishment of a separate, dedicated pathway for nanomedicines and their follow-on products would ultimately provide the highest degree of clarity and guidance for developers of originator and follow-on products, and the necessary assurance of comparability and reliability for health care professionals. This new pathway could be based around the concept of similarity (nanosimilars) along the lines of the existing approach to biologics, including requirements for traceability.

We understand that this might be beyond the scope of this strategy. Therefore, we propose improving the guidance for the implementation of the current regulatory framework: for the hybrid pathway to function effectively for nanosimilars, EMA would need to develop more extensive guidelines covering all nanomedicines beyond the four specific scientific guidelines for product areas that have been developed to date.

Regulatory clarity in this area coupled with appropriate monitoring, traceability and pharmacovigilance of follow-on products would help better ensure patient access to efficacious and safe copies of nanomedicines.

Second choice (h)

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

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.

Especially for smaller and mid-sized companies, the possibility of having continuous advice along the development process is fundamental in ensuring patients can have access to life changing and safe treatments as soon as possible.

Vifor Pharma has extensively collaborated with a partner participating in the PRIME scheme. We would encourage the continuation of PRIME and similar initiatives which provide a platform for early engagement between industry and regulators but also patient representatives, HCPs, HTA bodies and payers.

Access to early consultation and feedback from regulators prior to submission is extremely valuable in order to build quality dossiers and to anticipate challenges. An ability to have more regular dialogue beyond the relatively bundled and infrequent interactions of periodic scientific advice applications would strengthen the ability of applicants to make quality development choices as needed and to avoid committing to choices which ultimately lead to inefficient regulatory outcomes.

Third choice (h)

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

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.

Developing real world evidence is becoming ever more important, however RWE is not always accepted by regulators and/or payers, especially not with a consistent approach.

We believe that the EMA should launch a strategic initiative to integrate RWE in drug development to support regulatory approval. RWE is all too often a post-approval activity focused on pharmacoeconomic questions to evaluate effectiveness for pricing and reimbursement. RWE could potentially play a more significant part in evaluating efficacy for approval and in structuring drug development programs to yield beneficial health solutions at the time of initial availability. However under current regulatory frameworks incorporating RWE into pre-approval research is a complicating factor that can introduce delays and cost rather than an enabling factor for generating evidence to support regulatory decision making and accelerate availability to patients.

An appropriately directed strategic initiative on RWE could focus on clarifying the scope and quality of sources, approaches towards governance and handling of real world data underlying the observations, potential models for evidence generation and hypothesis testing required for utilizing these sources to support approval, and identifying where gaps exist.

The initiative should also contribute to extend the standards and methodologies for collecting, analyzing and validating RWE use internationally. This could be strengthened by parallel or coordinated activity via the ICH.

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

We believe that there should be a clear definition of nanomedicine in order to avoid confusion between nanomedicines, the use of nanotechnology in medical devices and the application of nanomaterials in manufacturing medicines. An increasing number of nanomedicines are about to lose patent exclusivity, becoming candidates for introduction of follow-on products. It would be beneficial if the EU would follow its own best practice from the recent past, notably the introduction of the dedicated marketing authorisation procedure for biosimilar products, where the regulatory approach was successfully defined, elaborated, and introduced by the EMA before follow-on versions were submitted for approval. This has proved successful in both protecting the safety of patients and in promoting further high-quality science in the development of the follow-on products and the EU has ensured a biologic medicines market that is both safe and exposed to competition. In contrast to other regions, the EU sees vast investments made in biosimilars, driven by a clear approval process, incl. definitions and guidelines. A 'similar' approach could help boost Europe's competitiveness in the nanomedicines field while ensuring patient safety.

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**:

28, 29) In light of the scientific complexities posed by the field of nanomedicines it is essential that the EMA fosters collaborations and network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science and to continuously improve regulatory approaches to adapt to technological developments.

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