Contribution ID: 4e4d60f8-66e8-48b3-b6de-9fb9e3af25c3
Date: 12/06/2019 13:18:43

Public consultation on EMA Regulatory Science to 2025

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* Name

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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:***

between 1 and 1 choices

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

Name of organisation (if applicable):

Takeda Pharmaceutical Company Limited

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 period up to 2025 will be a transitional period in the EU as a number of major events will occur (Brexit, EU elections and new Commission mandate) coupled with the rapid advances in science (new technology, new evidence, growing global community). This will require significant changes in regulatory science and it is important that going forward there is a balance in near-term progress and long-term direction in terms of strategy.

The increase in new technologies (e.g. Advanced Therapy Medicinal Products, gene therapy, digital health) and new modalities for drug discovery and development (e.g. Artificial Intelligence, in silico studies) will only increase over the next five years. When developing and implementing the EMA Regulatory Science Strategy, it is important to remember that the direction, priority and future skills required coordination with the EU national competent authorities and HMA. These will not be successful without being incorporated and coordinated within their Multi-Annual Work Plan.

The five strategic goals mapped out in the draft Regulatory Science Strategy address important priorities for the advance of medicines and therapeutic care in Europe. Key to the success of the recommendations is to realization that they are intimately tied together and cannot be implemented as such.

Our overall top three priorities are nested in each of the first three strategic goals (1 Catalysing the integration of science and technology in medicines development; 2 Driving collaborative evidence generation – improving the scientific quality of evaluations; 3 Advancing patient-centred access to medicines in partnership with healthcare systems). These top priorities are:

Foster innovation in clinical trials.

o Given the increase in ATMPs, particularly in the area of Rare Disease, the development of innovative trial designs to accommodate the development of treatments such as gene therapy will be key in delivering new therapeutic treatments in a timely manner.

o This initiative will also overlap with other priorities which encompass new clinical evidence sources (RWD and Big Data), measures (endpoints and biomarkers) and methodologies (Modelling and Simulation).

o It is important for the innovation to be cascaded down into the regulatory approval system for CTAs and ensure that there is consistency in the decision making.

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

o Flexibility and the coordination of advice needs to be reflected given the changing pace and process of innovation along the development continuum.

o This extends beyond the EMA initiated programmes (eg PRIME) and needs to bridge the gap to advice and decision making by national competent authorities. The process of development advice needs to

facilitate the bring together the output given at multiple points in the drug development and manage conflicting views. This needs to be done in a more holistic manner. With the challenges in the global nature of development, particularly within the rare disease environment and ATMPs, it is essential that this coordination/integration aims towards convergence on a global basis.
o The process needs to ensure the systematic engagement of the wider group of stakeholders (patients, HTA, HCPs).
Promote the use of high-quality real-world data (RWD) in decision making.
o There is a need to better define/address within a contextual framework novel sources (including digital), global standards and methodologies, and novel analytical techniques (e.g. AI, modelling).
o Key to the development of high-quality RWD is the use of digital health technologies. These will allow the gathering of data which is key to demonstrating safety and efficacy in "normal use" for both the regulatory authorities as well as the HTA bodies and payors.
o It is essential that the EMA engages in the forefront of the research in this area and defining the practical global implementation.
o It is essential that all key stakeholders are involved (patients, HTA bodies, industry, academics and HCPs) to ensure that the outcome addresses the real medical needs.
Our top priorities address the most urgent recommendations which we see as bringing innovative new treatments to European patients, particularly in the rare disease environment. However, the other elements of the strategy are also required for the EMA to be able to meet the challenges of the rapidly developing science. This is particularly relevant for ATMPs including gene therapy.
In addition, it is vital that the strategy going forward results in access to novel treatments for the patient not simply approved products. It is important to facilitate increased coordination/convergence in decision-making between regulatory authorities, HTA bodies and payers. The EMA has made great strides in this area but more efforts are needed to bring convergence to endpoints to allow both authorization and access.

Question 4 (human): Do you consider the strategic goals appropriate?

Strategic goal 1: Catalysing the integration of science and technology in medicines development (h)

- (●) Yes
- ( ) No

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

- (●) Yes
- ( ) No

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

- (●) Yes
- ( ) No

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

- (●) Yes
- ( ) No

Strategic goal 5: Enabling and leveraging research and innovation in regulatory science (h)

- (●) Yes
- ( ) No

Question 5 (human): Please identify the top three core recommendations (in order of importance) that you believe will deliver the most significant change in the regulatory system over the next five years and why.

First choice(h)

9. Foster innovation in clinical trials

1st choice (h): please comment on your choice, the underlying actions proposed and identify any additional actions you think might be needed to effect these changes.

Innovation in clinical trials often comes from the availability of new datasets (e.g. data captured by wearables, inclusion of “omics” technology) and stratification of patient populations into smaller populations by higher personalization of medicines which requires different trial designs and statistical methodologies for assessment of the data. Also shifts from symptomatic treatment to diseases modifying drugs may require other than the conventional endpoints and surrogate biomarkers.

Supporting recommendations to foster innovation in clinical trials are:

- Develop regulatory framework for emerging digital clinical data generation (10)
- Support developments in precision medicine, biomarkers and “omics” (1)
- Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products (5)
- Reinforce patient relevance in evidence generation (17)

Key actions:
The actions proposed above should be implemented to further this recommendation. It is important note that this is an opportunity to address some of the current inflexibilities in the regulatory approval system for CTAs.

We additionally propose as a key action that the Agency develops a new strategic initiative on complex innovative clinical trial designs (including adaptive design and master protocols) and involves relevant stakeholders (developers, patients, clinicians, regulators, HTAs and payers). By implementing a dedicated pilot programme this would increase the regulators experience with submission of such studies and facilitate the use and acceptability of such innovative clinical trial approaches by all involved bodies and stakeholders.

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.

This recommendation aligns with our vision of patients/trust/reputation/business.
EMA has already increased patient involvement in its various committees.

The recommendation supports other recommendations including
- Foster innovation in clinical trials (9),
- Develop the regulatory framework for emerging digital clinical data generation (10)
- Invest in special population initiatives (12)
- Contribute to HTA´s preparedness and downstream decision-making for innovative medicines (15)

Patient reported outcomes are important, especially in rare diseases or diseases of high unmet medical need where no long-standing established clinical endpoints for trials exist. Paediatric outcomes reported by their caregivers and a focus on special patient populations are also essential to advance development. Among the key actions, the inclusion of PROs into scientific guidelines and involvement of patients in PRO validation are particularly important. Please refer also to the proposed additional key action under “foster innovations in clinical trials” (first choice) with the involvement of patients into the strategic initiative on complex innovative clinical trial designs.

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.

While real-world data are already used in post-marketing safety surveillance and data collection, they could have additional importance pre-authorization and for HTAs and payers. Alignment between the different bodies for the development plan of a product is essential. RWD need to be addressed in the context of novel sources (including digital), global standards and methodologies, and novel analytical techniques (e.g. artificial intelligence, modelling).

Supporting recommendation include:
- Develop network competence and specialist collaboration to engage with big data (19)
- Contribute to HTA´s preparedness and downstream decision making for innovative medicines (15)
- Reinforce patient relevance in evidence generation (17)
- Exploit digital technology and artificial intelligence in decision making (14)
- Foster innovation in clinical trials (9)

Key actions to propose:
Seek to align and contribute to extend the standards and methodologies for collecting, analyzing and validating RWE use internationally. This should also incorporate the current recommendations under consultation in the discussion paper “Use of patient registries for regulatory purposes – methodological and operational considerations”. We recommend undertaking pilots to gain practice, including both retrospective and prospective case studies.

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

None identified.

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:

Although many guidelines for ATMPs already exist, at there are few products licensed up to now and many new treatments under development by a large number of companies. Consequently, experience gained during the assessment of the initial MAAs as well as the scientific/regulatory advice process will need to be integrated into existing and new guidance.

The identified actions all appear to appropriate to move forward this recommendation. Of importance, is the involvement of HTAs in the scientific advice process.

In order to support innovation, particularly in the rare disease space, it is important not to interpret similarity too restrictively in the context of orphan designations. This becomes particularly important with the increasing development of new treatment modalities such as gene therapy where the treatments have the potential to be curative rather than disease modifying.

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**:

This is a core strategic goal for medicine development and approval. Within it, the following recommendations are a priority from our point of view:

- Foster innovation in clinical trials
- Develop the regulatory framework for emerging clinical data generation
- Optimise capabilities in modelling, simulation and extrapolation
- Exploit digital technology and artificial intelligence in decision making

Lower priority is given to:

- Leverage novel non-clinical models and 3R as this is ongoing work internationally and much has already been achieved
- Expand benefit-risk assessment and communication as again much has been achieved and this is ongoing work. EMA is encouraged to continue current initiatives and collaborate with HTAs and national authorities.

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**:

Initiatives to advance patient-centred access to medicines in partnership with healthcare systems are an essential strategic goal.

Key priorities among the proposed initiatives are in our view:

- Reinforce patient relevance in evidence generation
- Promote the use of high-quality real-world data (RWD) in decision making
- Develop network competence and specialist collaborations to engage with big data
- Contribute to HTA´s preparedness and downstream decision-making for innovative medicines

We acknowledge that EMA cannot prioritize all recommendations and therefore suggest that new efforts be focused on the recommendations listed above. The recommendations listed below are already underway and therefore we suggest that they continue but not be the prioritized. These are as follows:

- Deliver real-time electronic Product Information
- Further develop external communication to promote trust and confidence in the EU regulatory system (which is already established we believe and should be maintained)

In addition, there are a number of recommendations that while important are primarily the responsibility of other groups. These should not be a key focus for the EMA but rather there should be participation where appropriate. These are as follows:

- Promote the availability and uptake of biosimilars in healthcare systems
- Bridge from evaluation to access through collaboration with payers

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**:

This strategic goal is fundamental to EMA´s mission. To a certain extent, the relatively lower priority given to the recommendations in this section reflects our view that these are ongoing priorities that the Agency must maintain and not new innovative strategic goals.

From an industry stakeholder´s perspective, we give the greatest priority to:

- Support innovative approaches to the development and post-authorisation monitoring of vaccines and
- Promote global cooperation to anticipate and address supply challenges.

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**:

We support the development of network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science and share knowledge and expertise. However, it is important to ensure the inclusion of pharmaceutical industry researchers into these initiatives. There is a significant amount of expertise retained in industry R&D departments which allows for the translation of research ideas into new treatments for patients. Much of this translational expertise is not found in academic research institutes.

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