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Public consultation on EMA Regulatory Science to 2025

Fields marked with * are mandatory.

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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

Name of organisation (if applicable):

ISPOR - The Professional Society for Health Economics and Outcomes Research

Question 2: Which part of the proposed strategy document are you commenting upon:

- (•) Human
- ( ) Veterinary
- ( ) Both

Question 3 (human): What are your overall views about the strategy proposed in EMA's Regulatory Science to 2025?

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

ISPOR – the Professional Society for Health Economics and Outcomes Research - is pleased to respond on behalf of its membership to the EMA's consultation on "Regulatory Science to 2025." We strongly agree that these are important issues to address with input from a wide variety of stakeholders, and thank the EMA for this opportunity to provide our comments.

ISPOR is a scientific and educational society with many of its members engaged in some aspect of health economics and outcomes research (HEOR) related to evaluation of pharmaceuticals. Our membership includes over 20,000 individuals across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

We created an online survey for our members to rate each of the 31 core recommendations from "very important" to "not important", as in your online questionnaire, and allowed for verbatim comments in each section as well. Our response to your online survey reflects the combined responses of 204 respondents, of whom 46% work in Europe. Among all respondents, 35% work in academia, 26% work in the life sciences industry, 17% in health research consulting, and the rest is balanced in other sectors such as clinical practice, government, private payers, or patient organizations. 93% responded personally and 7% on behalf of their organizations. To select the 3 most important core recommendations we selected the three which had the highest rating for "very important". To rate the individual core recommendations we used the median response, meaning that to rate "very important", at least 50% of the respondents had to rate it as "very important." We include verbatim comments provided by respondents for your consideration – these are not "consensus" ISPOR comments, however.

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)

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

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.

Nearly 69% of our survey respondents marked this as "Very important", with another 24% marking it as "important." Use of real world data has long been of keen interest in health economics and outcomes research, given that both the economics of health care and the actual outcomes of treatment are fundamentally real-world/real-life phenomena.

Second choice (h)

15. Contribute to HTAs' preparedness and downstream decision-making for innovative medicines

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.

56% of our survey respondents considered this "very important" and 34% rated it important. HEOR and HTA are closely linked areas of work.

Third choice (h)

2. Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments

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.

53% of our survey respondents marked this as very important and 37% rated it as important.

Virtually tied for third place in our survey was recommendation 31 "disseminate and share knowledge, expertise, and innovation across the regulatory network and to its stakeholders."

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

None that we 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:

Comments provided by our members included:

- (Goal 1) Science is a broad term. In the regulation of medicines and healthcare, society misses integration of social sciences and its methods (e.g. ethnomethodology) to ensure patients' and populations' perspectives are appropriately and fairly integrated.
- Evaluate clearly the net advantages of development of technology in medicine
- (Goal 2) Support translation and help to clarify the P&R process, in that it isn't always so clear or defined.
- (Goal 1) Number 4: History has shown that the best way to lower the cost of treating patients in the long run is to apply innovative manufacturing technologies to the question of cost.The greater the technological efficiency for treatment production, the lower the overall cost to treat patients. In the arena of ever increasingly precise biological identification/diagnosis of disease and mechanisms of action, the pool of homogeneously identified diseases becomes ever more fragmented and specific. Hence, the notion that; if parsed enough, most diseases could become classified as 'Orphan Diseases'. The technologically specific production of treatments and cures for highly specified diagnoses has not kept pace with the rapidly growing ability to narrowly specify a disease, or subcategory within a disease family. Specificity of identifying diseases and their treatment must be matched with the economical efficiency of production and distribution of the treatment to the patient. If not, societies will be left staring at treatment and cures that are dangling out of reach from patients and physicians along with those responsible for payment.
- (Goal 1) Focus should be on low cost developments. (Goal 4) Focus should be on lower cost but safer manufacturing technologies
- Start with a few new technologies to set up the roadmaps for integrating regulatory and reimbursement process into new product developments, for example, next gene sequencing, robotic surgery, and immunotherapy.
- Innovative technology is perhaps the need of health care. I recommend public health care for a transformation towards sustainable goals.
- In relation to no.2 and 4, therapy with cells and tissues will be much discussed for the patients to be able to have the same therapy around the world, and for the industry to be able to discuss manufacturing process of the product in the line with the based perspectives among EMA, FDA and PMDA.
- 7. The provision of research cost and price could be introduced here.
- 4. Rather than promoting novel manufacturing techniques, I advise to focus on evaluation of techniques available in a specific country for their quality and adopt as a country. If we follow always novel techniques, then the development of more reliable techniques will be less. So develop more specific and quality technique and evaluate it.
- Equally important as #6: develop understanding and regulatory response to digital health interventions, especially to AI/ML approaches
- Process improvements, aligning the regulatory with research, manufacturing and other technology - enabling stakeholders will be critical to accelerating the product development life cycle. This in turn will sharply reduce time to reach productive Go/No-go decisions and reduce costs for development. Integration of devices, diagnostics, patient preferences, and technology to improve selection of the likely responders and adherence by patients to care also should be considered much earlier on in the development process.
- Main priority is advancing understanding of why there are unmet needs, what translational priorities fill the associated gaps and what technologies accelerate 'gap filling'. The emphasis is on target and focus.
- Point 1 - It is unclear what is meant by support developments - does this mean that all fees are waived? OR will sponsors be supported by the EMA by having samples analysed free of charge and obtaining statistical analysis and AI support or validation? Point 4 - within the EU by which means? Point 7 - The integration of regulatory advice is only of importance if the EMA is willing to make contractual obligations and decisions that do not leave sponsors with the risk.
- Point 5 should include dressings too

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**:

Comments provided by our members included:

- #9: Innovation will be fostered by manufacturers as they have incentives to do so. Regulators should focus on their mission of safeguarding the interests of the EU population whilst maintaining an open attitude to innovation and contributing with scientifically valid solutions.
- 10 & 14: Need for a framework able to support assessment on the quality of digital data and digital data sources (validity and reliability must be demonstrated in many cases)
- 10, 14 - These will be particularly in need of guidelines in the European setting with regard to GDPR compliance. Difficulties may otherwise be encountered by innovators who will need access to primary data, but run the risk of huge fines for accidental or negligent data mishandling.
- Point 12 - this is a sponsor market driven decision it is unclear why the regulators would which to invest in sub-groups unless this is part of PRIME, i.e. unmet need - thus appears contradictory. Point 14 - Digital technology in decision making requires detailed regulatory attention and regulations and guidelines.
- Goal 2, number 14. I agree that exploiting digital technology and artificial intelligence in decision-making is important. What I fear, from personal involvement of building and implementing decision-making models, is not the model itself. But, executives, managers, and administrators that have already become too enamored with decision-making models and have disregarded many of the sound rules for building, implementing, reviewing results of, and revising models based on a continuous review of the validity of the underlying model data, let alone assessment of a shift or drift in the new incoming data. Failure to continually observe my rule number one, "Know Thy Data" will gradually steer you off course without you realizing it. In the navigational world, navigators continually adjust their magnetic compass headings based upon where they are in the world. We are still in the magnetic compass world of artificial intelligence assisted decision-making in healthcare. Until we evolve into a GPS world of data, some healthcare evaluation and payment organizations will allow themselves to be 'steered off course' with negative consequences for patients, providers, and other organizations associated with delivering and paying for healthcare.
- Important for the EMA not to be driven by what the pharmaceutical industry wants rather than what is best from the perspective of the community who want to be able to trust that medications they use are both safe and effective.
- Again, begin with some disruptive products to set up the roadmaps. AI and digitalized medicine is the big trend in clinical decision making. Large data, digital data are way more valuable in medicine than controlled, small sample size trials. The key is the quality of the large data analyses. In regulatory, encourage the use of large data and apply the appropriate method is critical.
- In relation to no.9 and 14, the weakness of RCT, such as generalizability, will be discussed to compare with RWD, in such case, we can make use of AI technology for the comparison.
- 11. Patient-centeredness is poorly defined in regulatory science. To be relevant for evidence-based decision making, the preferences of well-informed should be rigorously quantified and validated. Decisions involving benefit-risk assessments are likely to be the most preference-sensitive and the area of most relevance for quantitative preference data.
- AI has huge potential to filter through data for better predictive modelling and results.

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**:

Comments provided by our members included:

- #16 is likely to clash with EU member states' sovereignty in prioritization and allocation of (healthcare) funds. Ensuing recommendations from HTAs is likely less contentious. #17 FDA's Guidance on the development of Patient Reported Outcomes is a good example of how to appropriately integrate patients' perspective; try to ensure that patient comments are at least somewhat representative. #19 Please do it in the specific context of scientific discussions of therapeutic development plans. Please do not try one regulation "fits all". #22 Despite notable efforts, it should be noted that external communication by the agency is still cryptic.
- Increase the role of experienced patient experts in these processes. Involve patient experts in the development of health economic models. Patient centeredness should be part of any work done.
- Though all cited parameters are important for better outcomes, I believe that development of networking with availability of biosimilars in each society are important along with better understanding of the individuals.
- 18. Very important as results obtained in highly focused and structured RCTs (currently the focus of HTAs) is often not replicated in common practice, where resources may not exist to reproduce the care conditions of a study. Decision-makers and end users should have access to more realistic data to temper expectations for technology or pharmaceutical performance "in the wild" 22. In the case of limited resources, I would suggest this is less of a priority as EMA is already rather highly regarded and doesn't require specific investment in promotion.
- 16. Collaboration with payers should be through pressure to lower prices and not impede entry of generics after patent expiry 18. Real world data cannot be used until many years after new intervention entry - implement long-term efficacy follow-up similar to long-term safety follow-up for new interventions.
- 16. Collaboration with payers should be through pressure to lower prices and not impede entry of generics after patent expiry 18. Real world data cannot be used until many years after new intervention entry - implement long-term efficacy follow-up similar to long-term safety follow-up for new interventions.
- Point 18 - The inclusion of RWD should strive for a mandatory data set that is agreed upon with the HTA/payers.
- Goal 3, number 19. Need to be aware that networks of collaborating specialists develop a group think perspective and approach over time. To avoid this, perhaps, a 'Skunk Works' approach should also be proffered. This would provide for disruptive skepticism to the current way of doing things. It could also provide a leapfrog approach to advancing patient-centered access to medicines in partnership with healthcare systems.
- 15 and 16: these are very important if the regulatory recommendations are seriously considered and implemented by decision makers and payers.
- While section 3.2.4 seems to refer the most to the use of patient preferences, it is in a very general way and refers to another section (3.3.3) where “preferences” are not mentioned. In this section (3.3.3) it is not clear if reference is made to preferences or other types of data/methods. It would be very helpful to have some clarification on this matter. Hereby an overview of mentioned sections: 3.2.4: Expand benefit-risk assessment and communication Actions: “Expand the benefit-risk assessment by incorporating patient preferences” 3.3.3: Reinforce patient relevance in evidence generation. Actions: “While validating PROs, address patients' needs and leverage patients' expertise” “Explore additional methodologies to gather and use patient data from the wider patient community during benefit-risk evaluation.”
- 15.: Sometimes there are special impacts of the legal, ethical and organizational domains in HTA. There are methodological issues but the framework has to be developed with a consensus on societal level.
- RWE/D is patient-centric but that doesn't mean that patients are involved: this seems just a definitional fudge. The information gap is that decision makers are constrained against the tidal wave of innovative meds by affordability and sustainability. I'm less inclined to prioritise 'administrative' priorities such as networks. Nice Euro-speak and keeps everyone happy with committees, but the issue is the payer challenge regardless of how framed. Compelling results do not on their own make the case for being patient centric.
- Pointing to biosimilars is missing the point. Original biologicals have long patent lives, so patients have to wait too long; then biosimilars also are high priced compared to other off-patent products.

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**:

Comments provided by our members included:

- 25. Global cooperation is necessary and is the key to anticipate and propose the most common responses.
- Support the development and implementation of a repurposing Framework. This task is not even feasible, and unclear how it would even be approached and what the outcome or purpose would be. Seems like one of these topics where money will go straight down the drain because everyone will be "working" on nothing just for the sake of Funding.
- 26. Why just vaccines - should monitor all interventions post-authorization for both safety and efficacy.
- Point 24 and 26 require the set-up of sentinel sites that have well trained and dedicated staff that can deliver high quality data.
- We may have less discussion on supply chain of the mdical products including successive production, and also supply vaccines in the world.
- 24. I advise please don't focus on development of new anti-microbial agents more because again those antimictobial agent will be introduced in huge amount and cause resistance. Better to plan how to use it in real-time and plan to avoid use of anti-microbial agents in vegetable or fruits.
- All important, none is a standout for me. The general point is incentivise repurposing (old things can be novel), and where we know there is a misdirection of pharma industry priorities through lack of incentives: the real AMR threat is the lack of interest.
- I don't know what you mean by "ring-fence" resources. Please avoid jargon. I am assuming you are talking about containment. Also, you should have Not Sure or Don't know as an answer choice, also you need a negative response option. Finally, re supply challenges, EU policies and practices should not depend on global cooperation. Nice if it can happen and be meaningful, but cannot count on it. E.g. Gavi only supports pilots, but now all the African countries depend on Gavi (NO COUNTRIES have ever "graduated" from Gavi as was the intent of Gavi programs, and thus have not developed their own immunisation systems and supplies. Finally, I am not sure of what you mean by a "repurposing framework".

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**:

No comments here.

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