PATIENT FOCUSED MEDICINES DEVELOPMENT

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Public consultation on EMA Regulatory Science to 2025

What are your overall views about the strategy proposed in EMA' s Regulatory Science to 2025?

Patient Focused Medicines Development (PFMD) welcomes the opportunity to comment on the strategy proposed in EMA's Regulatory Science to 2025. PFMD is an open, independent and global coalition of health stakeholders that aims to transform the way in which we understand, engage, and partner with patients in the design and development of research and medicines by focusing on patient needs and priorities. PFMD brings together and synergizes disparate but complementary efforts that integrate the voice of the patient across the lifecycle of medicine and currently has 32 member organisations including patient organisations, pharma/life sciences industry, academic, regulatory and health technology assessment organisations.

Patient engagement is moving apace. Ensuring that EMA's strategy is future-proof with clearly defined expectations and measurable criteria for meaningful engagement with patients is imperative if patient engagement is to become the 'norm' by 2025. As such, we believe that the language within the proposed strategy should reflect this advancement: in every instance where 'patients' are noted, it will be important to assess whether the proposal is meeting EMA's intention to work **with** patients and not just **for** patients.

In relation to the human sections of the proposed strategy, we commend the overarching commitment to improving meaningful patient engagement to ensure that the patient voice is not just heard but listened to and acted upon in EMA regulatory processes. At DIA Europe 2019, Guido Rasi (EMA Executive Director) was reported as confirming EMA's intent "to make patient engagement the norm by 2025". If this objective is to be realised, we believe that the proposed strategy should go a step further and be more specific in what is expected from stakeholders in terms of patient engagement. We would propose clearly identifying (and, if necessary, mandate) expected standards, activities, outcomes and metrics to provide concrete guidance for the many stakeholders who are committed to meaningful patient engagement.

We believe that taking a more proactive and directive approach (such as that used by the FDA) will deliver the needed change much more effectively. Without setting clear expectations towards those submitting dossiers and updates to EMA, patients at best can filter or comment a bit, and it would be difficult to fundamentally increase the patient value of what is submitted. We believe that EMA should expect and strongly encourage patient input into the studies that form the backbone of their submissions. This could be achieved by insisting for more patient engagement in the content creation of the document (such as studies, reports, and patient-reported outcomes [PROs]), and in being more specific about what is required to fulfil EMA expectations in this regard. For example, we would propose that EMA clearly states that every study should evaluate the need for PROs in addition to the classical medical scientific outcome parameters. Such a PRO should be proven to be relevant to patients and tested with patients for acceptance and ease of use.

In addition, we would propose that EMA requests that every submission justifies the outcomes presented as relevant to patients based on their qualified and quantified views, not just on how doctors see the need. Although the current proposed strategy implies or infers this, we believe that it should be made explicit so that it is an integral part of the process that cannot be avoided and that there is no opportunity to develop submissions without asking for patient engagement. For example, EMA could clearly state that they expect (documentation of the fact that) patients have been involved in (1) the design, (2) the implementation and (3) the interpretation of all pivotal studies in a submission dossier. Peer-reviewed scientific journals such as the British Medical Journal are already projecting the same expectation to publish studies in the future, so the EMA request would be totally aligned with this growing movement, and very specific.

Importantly, regulatory bodies such as EMA are in an ideal position to extend their influence beyond their immediate sphere, taking a leadership role to ensure that patient engagement becomes the norm across diverse stakeholder groups and ultimately the whole healthcare system. The value of including patients as partners in the design and development of treatments is increasingly recognised, because engaging patients can result in solutions that better meet needs, improve health outcomes and speed up development.

Importantly, regulatory bodies such as EMA are in an ideal position to extend their influence beyond their immediate sphere, taking a leadership role to ensure that patient engagement becomes the norm across diverse stakeholder groups and ultimately the whole healthcare system. The value of including patients as partners in the design and development of treatments is increasingly recognised, because engaging patients can result in solutions that better meet needs, improve health outcomes and speed up development.

This is a mind shift of the same magnitude as advances in science and technology that improve and transform research for the benefit of all stakeholders. In order to nurture this shift, the regulatory science and framework must advance in tandem and acknowledge the importance of involving patients as being essential to achieving more targeted, safer and more effective treatments. The FDA's regulatory framework with the Prescription Drug User Fee Act V and VI, then with the 21st Century Cures Act and its ongoing work to improve the way patient input can be incorporated into research and development of medicines, is an example of the changing times and the regulatory adaptations that we believe must follow.

EMA aims to develop and internationally harmonise methods and standards in regulatory science via a multi-stakeholder platform. Collaboration with established and known partnerships will bring the multi-stakeholder focus and co-creation that focuses on bringing the patients voice systematically from beginning to end in all processes. EMA's proposed strategy highlights the global nature of medicines development and the importance of collaboration in achieving common objectives. This is a welcome focus that will allow cross-fertilisation of approaches, ensuring efficiency and timeliness in reaching EMA's objectives for patient engagement. For example, in the approach to development, alignment and implementation of guidance for capturing patient insights for file submission and leveraging insights from initiatives such as the development of Clinical Outcome Assessment (COA) guidance by the FDA. EMA's proposed strategy also touches on emerging health threats. Again, international cooperation for preparedness and coordinated response will be crucial and facilitated by the global collaborations that will be established to harmonise regulatory processes and deliver timely and effective solutions.

Also highlighted in EMA's proposed strategy is the increasing complexity of medicines development and the regulatory challenges this brings. The demand for health economics data, increase in interest in drug safety data, and shift toward personalized medicine, has led to an explosion in the amount of data being generated in a clinical trial due to increasing protocol complexity and requirements to collect additional data. There has been an increase in the number of study end points, procedures required to support end points, and data collected from patients. Patients can help to meet these challenges for example by helping regulators and sponsors understand what really matters (indications, end points), providing input into risk/benefit assessments and PROs, providing guidance on realistic inclusion/exclusion criteria (based on experiential knowledge and insights from people living with the condition being studied) and raising awareness of the importance and relevance of clinical trials.

Do you consider the strategic goals appropriate?

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

"No", as it is currently stated, but "Yes" if the science and technology also take into account the need for meaningful patient engagement. We believe that the classical chemical, biological and medical sciences are limited without adding the patient perspective. Technology can be a huge enabler (examples of digital empowerment through AI, sensors, apps etc) are all around us. But we need the Science of Patient Engagement to develop and to set the standards of how and when to engage, of how to collect and interpret patient data, of how to measure patient relevant parameters. From the patient perspective, these objectives are key. The strategic goal would be strengthened and more comprehensive if revised to pertain to both classical and patient sciences.

Furthermore, a deep understanding of patient needs and priorities (including what is acceptable 'risk') is required in achieving EMA's objective to ensure that regulation can support the development of new medicines and innovative technologies that address patients' needs better with safe and clinically appropriate treatments, in order to deliver more patient-centred healthcare and personalised medicine.

Focusing only on developing a closer collaboration with academics, research centres and infrastructures alone is unlikely to deliver the outcomes desired by EMA. We believe that the recommendations or actions suggested in Goal 1 need to more comprehensively reflect that patients are a critical piece of the puzzle in achieving the stated goal. Mention of patients should not be restricted to the need for more impactful external communication for increasing awareness for the PRIME scheme.

While prioritising the improvement of understanding of and regulatory response to emerging new manufacturing technologies, borderline products and innovation, patients should be considered as an integral part in the improvement considerations from early research to evaluation discussions. Patients' views and perspectives should also be integral to and inform plans to adapt evaluation procedures as suggested and all decision-making process that will ultimately affect treatments for patients.

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

As above, "No" as it is currently stated, but "Yes" if improving the scientific quality of evaluations concern patient engagement. We believe that it is paramount to involve the patient community together with other stakeholders when it comes to innovating and adapting the clinical trial processes to fit modern challenges and needs.

While the proposed actions in the strategy document suggest working with stakeholders to encourage collaborative clinical trials, we would propose improving it in two aspects. Firstly, we would propose including patients as one of the stakeholders to engage with.

Secondly, we believe that fostering innovation should extend to the way regulators think about the role of the patients and their contribution in driving change and innovation, in designing good clinical practices, in clinical data generation, in benefit-risk assessments, in facilitating the regulators' communication with and access to special populations and in building the capacity and capabilities for regulators and other stakeholders to tap into a rich data source (of patients' lived experience) that should be at the centre of efforts and strategies to improve public health.

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

"No" as it is currently stated. The EMA proposes to increase cooperation with other regulatory bodies such as the HTA and payers, but does not mention the importance of patient input in the decisions made by these bodies. Mention of patient engagement appears to be restricted to input and data generation and as a resource. We believe that this omission fails to reflect the need and value for meaningful patient participation and incorporation of patient perspectives into these decisions.

New standards and guidelines proposed within the strategy should also be co-designed **with** patients to ensure that the patient perspective flows through the entire process, which will then ensure that effective and needed treatment will not face the barriers (such as delays in reimbursement decisions) they otherwise might face without the patients' input in the discussions early on. By including patients throughout, the aim is to make medicines available to patients faster, and to develop medicines that better meet patient needs to improve health outcomes.

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

"No" as it is currently stated. The intention to involve patients more in scientific committees is commendable. However, there should be specific proposals and recommendations defining how patients will be an integral part of the decision-making process in addressing emerging health threats and therapeutic challenges.

The approach and process describing how the patient perspective will be captured and embedded in these processes should be explicitly described and made granular within the proposed strategy.

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

"No" as it is currently stated. As currently described within the proposed strategy, "regular, iterative engagement is required between regulators, funders, and academia…" to achieve this goal. However, we believe that the stakeholder groups should be widened to include engagement with patients and to ensure that the EMA's approach will be beneficial to the end users, the patients.

Furthermore, engaging only with academia in designing regulatory training modules will not deliver innovation and will not lead to faster and more effective medical breakthroughs if the patient perspective is omitted. Involving the patient community and training stakeholders on how to utilise relevant and high quality patient input is key to accelerating clinical trials, expediting vaccine development, improving market access rate and reimbursability, and improving trust and transparency towards medicines research, development and regulation.

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

The healthcare system has dramatically changed in the past two decades. Throughout history, physicians or the pharma industry took decisions for the patients. Today patients feel more empowered to take part in defining and developing medicines and care strategies. Industry and regulators realize that they need to work with the patients in order to better serve the patients' needs and desires. Patient engagement is becoming a reality not only for patient engagement officers and patient advocates, but for a variety of roles within healthcare organisations, and is being implemented systematically in many organisations. Patient engagement can be concrete, measurable and

PATIENT FOCUSED
MEDICINES DEVELOPMENT

successfully implemented if the conditions are right. In this context, key healthcare players such as the FDA are seeking to formalise and systematise how PE is done.

Today, isolated initiatives for meaningful Patient Engagement exist, but the approach is fragmented, and thus produces fragmented results. Organisations do not communicate with each other optimally, and work is sometimes duplicated or conclusions are contradictory. To serve the needs of patients better, and to achieve better health outcomes, we must transform the way in which we understand, engage, and partner with patients globally in the design and development of research and medicines by focusing on unmet patient needs.

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

There is a need for patient involvement in the governance models to be linked to real-world data (RWD). The tangible value of incorporating patient generated RWD, importance of patient registries that include clinical data and also quality of life data and outcomes that matter to patients should be highlighted.

A recent review of EU-funded initiatives for RWD generation provides insights and suggestions for how the outputs of these studies may be better incorporated into regulatory decision making (Plueschke et al. 2018). Ensuring that the patient perspective is routinely and appropriately incorporated through development and implementation of frameworks/guidance would further improve the value of RWD and the resulting regulatory decisions based on this data.

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)

PATIENT FOCUSED MEDICINES DEVELOPMENT

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

We believe that the whole lifecycle of medicine, from development to market access, should be facilitated through improved collaboration between patients and all stakeholders including payers. EMA is strategically placed to help make this happen.

The current FDA initiative to establish core, co-created sets of clinical outcome assessment and related end points is a good example of helping to define a common ground that reflects the patient perspective and which informs the whole lifecycle of medicine. Working with payers is the opportunity to develop core sets of COA that match not only the need of the regulator but the payer as well, making the whole process more coherent and cohesive and allowing a more sustainable patient engagement approach through harmonization and reduction of duplication of work and effort.

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.

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					

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					

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					
22. Further develop external communications to promote trust and confidence in the EU regulatory system					

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					

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

	Very important	Important	Moderately important	Less	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					