# Public consultation on EMA Regulatory Science to 2025

> Fields marked with * are mandatory.

**\* Name**

**\* Email**



# 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):*

GKV-Spitzenverband

**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 Strategic Reflection includes many important objectives for the EMA. Nevertheless, there is room for improvement.

The proposed strategy lacks a definition of key priorities but rather loses itself in details. These details are primarily driven by a firm belief in technology and the advancement of science and thereby neglect the prioritisation and definition of medical objectives and public health needs. Nevertheless, with regard to healthcare, technologies and scientific developments do not present a value in themselves.

EMA states that its mission is the protection of human health. The paper seems to be focused (almost exclusively) on ways to bring new products to patients as fast as possible, implicitly assuming that all new products have an added benefit for patients and/or health systems. The paper lacks a proper reflection of harms and risks. Indicative is the fact that – in difference to the veterinary part of the paper – the paper mentions pharmacovigilance only once. EMA seems to consider itself as a co-developer of medicinal products. This is a slippery slope as it may endanger EMA's primary task, being a regulator for providing effective and safe medicines. Speedy access must not come without proper evidence defining a new products place in therapy and ensuring that its benefits outweigh its risks.

In addition, the paper does not reflect on the fact that many new products have no or a very limited added benefit in comparison to current standard of care. It lacks conclusions, whether the current regulatory model is handling those drugs in a proper way. From a payer's perspective, these drugs are controversial. Although there are examples where me-too drugs could be utilised for the induction of competition in a patent-protected market, in general drugs that present only minor improvements but extremely high price tags put health care systems under strain. Therefore, such policy does not contribute to a higher level of healthcare but rather jeopardises current levels of healthcare protection and access.

The Strategic Reflection also lacks a critical reflection on the need for better quality clinical trials (at least randomisation).

Several reflections provided rely a lot on the feasibility of Big Data and so called Real World Data (RWD). Observational data, which is the preferable term for RWD, has always had its place in medical sciences. Many project in the fields of pharmacovigilance and healthcare research rely on observational data. Nevertheless, observational data is inherently prone to bias. Thus, instead of promoting the use of observational data for all research questions, one should first define questions that need to be answered, and then select the type of data that is suited best to answer them. In addition, currently neither the availability of healthcare related Big Data nor the methodologies to draw meaningful conclusions from it do meet the expectations proponents set in them. Even in 2025, correlation does not necessarily mean causality. This restricts the usefulness of those data for deciding whether benefits of a new medicinal product exceed its harms.

The Strategic Reflection conveys the idea that Big Data and precision medicine will be widely operational in the period leading up to 2025. In addition, the potential impact of new data generated throughout the life cycle should be critically discussed (e.g. re-assessments, withdrawal of marketing authorisation, safety alerts, changes in SmPCs).

The current strategy would appear to extend the role of EMA far beyond that of marketing authorisation decisions and its regulatory competencies to for example, biosimilar uptake, drug shortages, and data generation for downstream decisions. However, EMA's role in these processes must be limited to information sharing and facilitating better cooperation between the different stakeholders, including the payers and the HTA bodies, without impinging on their respective competencies.

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

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

- ○ Yes
- ● No

## Comments on strategic goal 1 (h):

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

EMA should clarify that

a) support of developments in precision medicine, biomarkers and 'omics',

b) translation of ATMPs into patient treatments,

c) promotion and investing in the PRIME scheme

are only useful, if these developments are targeted at public health needs and have the potential to substantially improve the health status of patients. Central marketing authorisation for "me-too" products can lead to improved competition (as we have seen with the new generation medicinal products for Hepatitis C), but products which do not offer a real benefit should not profit from incentives aimed at tackling high unmet medical need. We call for a more critical approach and greater transparency. While EMA needs to gain expertise to critically assess and evaluate new technological developments such as ATMPs, EMA's role – above all – is to ensure that only products with sufficient and appropriate data demonstrating their safety and efficacy reach European patients. Its role should not be driving innovation, but rather the critical evaluation of potential advancements for patients.

Regarding facilitating new manufacturing technologies, we agree that this is useful if it is linked to higher quality of the product and/or greater efficiency of the process.

We believe it is very important that EMA develops appropriate regulatory pathways for products associated with medical devices, in-vitro diagnostics and borderline products and strategies to deal with nanotechnologies and new materials in pharmaceuticals (as far as these products will be relevant by 2025). Nevertheless, these pathways need to build upon the most rigorous standards of assessments suitable for any involved product and must not be based on the lowest requirements.

Conclusion: the paper fails to focus sufficiently on the products that address public health needs and that truly warrant regulatory support.

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

◯ Yes

◉ No

## Comments on strategic goal 2 (h):

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

Importantly, EMA should maintain the requirement for high levels of evidence of efficacy and safety obtained from clinical trials (preferably RCTs) for all products where possible. This must be part of EMA's strategic goals.

However, increasingly technological developments and manufacturers are driving the development of new products aimed at small patient groups. This leads to a growing number of new products with limited evidence on efficacy and safety at the time of marketing authorisation. Therefore, collaborative evidence generation is needed. The focus should be on the best ways of generating Real World Evidence (RWE) by randomised studies, based on real world data (RWD). It must be clarified which data are appropriate to answer which questions.

Providing HTA and payers with better evidence is key for the future handling of those products. However, all participating parties need to be aware of the different duties and questions each stakeholder has to answer and respect these responsibilities.

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

○ Yes
◉ No

## Comments on strategic goal 3 (h):

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

> Payers welcome EMA's cooperation with HTA institutions, payers and manufacturers in early dialogues on products that have a potentially high impact on the health status of patients. This dialogue should be early, and it must be clarified how HTA data requirements and post-marketing evidence generation will be integral to obtaining market authorisation.
> Reinforcing patient relevance in evidence generation is indeed an important objective.
>
> So far, the possible use-cases for Big Data/RWD are more promise than fact and should be reflected in a more balanced way. The limitations of Big Data/RWD in terms of validity and utility in comparison to existing evidence standards have to be clearly addressed and a discussion about when and for what purposes this kind of data can be used has to take place. Thus, clear guidelines and transparent requirements need to steer these developments.
> Payers welcome the support of EMA concerning availability and uptake of biosimilar medicinal products. Trust in the EU regulatory system will improve if EMA takes a more critical stand regarding studies of manufacturers (e.g. demanding relevant comparators, validated surrogate outcomes …) and the expected benefits.

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

○ Yes
◉ No

## Comments on strategic goal 4 (h):

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

> Payers welcome the engagement of the EMA in emerging health threats (including AMR) as well as improving the availability of pharmaceuticals addressing these needs. Nonetheless, increasing manufacturing capacity in Europe, new business models and influencing vaccine decisions are not part of EMA's tasks, but require a political mandate. In contrast, fostering new approaches for the development and approval of vaccines is a welcomed objective. Instead of influencing vaccine decisions taken by healthcare systems, EMA has a more appropriate role in promoting sound scientific information on the efficacy and safety of vaccines.
> Repurposing is a promising field for further support, and we welcome the ongoing discussions in the STAMP on a possible repurposing framework. However, it should be avoided that the repurposed drugs acquire new intellectual property rights and significantly higher prices. Otherwise, it will endanger accessibility, even for those patients using the drug for the existing indication.

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

○ Yes

◉ No

## Comments on strategic goal 5 (h):

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

It is important for EMA to be informed about relevant scientific innovations and research in order to identify solutions to regulatory needs and challenges. This is fundamental to EMA's work rather than being a strategic goal in itself. In order to address the regulatory challenges, EMA needs to be active in scientific networks and interact with academia

Thus, it would be more appropriate to add a separate "methods" chapter where it is explicitly stated how strategic goals 1-4 will be achieved.

Concerning these research activities, EMA should further ensure complete transparency in all stakeholder involvement.

## 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)

11. Expand benefit-risk assessment and communication

## 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.

A more systematic application of the benefit-risk assessment methodology is highly welcome, especially an improved communication with payers and HTAs on suitable comparators, therapeutic context and outcomes. When patient preferences are increasingly incorporated, it has to be ensured that this is done in a methodologically sound, transparent and impartial way with clear rules for conflict of interest. In addition, the determination of patient preferences is methodological challenging; currently there is no scientific consensus on the relevancy of patient preference studies.

Regarding communication, EMA should publicly explain its decisions and provide insights into the benefit-risk balance, especially warning against possible harm so that patients are informed about side effects. EMA's decisions need to be as transparent and self-explanatory as possible, to enable downstream decision makers to correctly understand and work with the documents that are part of the decision. Thus, any ambiguity regarding the reasons behind decisions must be avoided and conducted analyses must be as thorough as possible.

## Second choice (h)

4. Facilitate the implementation of novel manufacturing technologies

## 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.

We are currently seeing the advent of bedside production, be it for monoclonal antibodies or cellular therapies. The current conditions for GMP manufacturing seem not to be sufficient for those technologies. To be sufficiently prepared, EMA needs to develop a framework for assessing medicinal products using those production routes that guarantees authorised products are safe and efficacious and of constantly high quality.

## Third choice (h)

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

## 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.

HTA is the basis for evidence guided reimbursement decisions. Thus, EMA needs to ensure that requirements for HTA processes are already integrated in the pre-authorisation phase. Trial designs should reflect the requirements of HTA assessments.

The fulfilment of HTA requirements must be essential for achieving MA. Whenever it is considered impossible to present sufficient evidence for the assessment of added benefits on outcomes that are relevant for patients at the time of approval, EMA needs to cooperate with HTA-bodies on which additional data will be required preauthorisation and how to address open questions post authorisation. It is crucial for healthcare systems to be able to justify the allocation of (usually) considerable amounts of public resources by valid evidence and thus avoid that access to this treatment is delayed.

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

The proposed strategy lacks a critical evaluation of EMA's current methods and potential adaptations (e.g. risk assessment/pharmacovigilance, conditional MA, withdrawing MA, orphan drug designation etc.).

It also lacks a critical evaluation of EMA's actual role, e.g. "co-developing" and the assessment of added value should not be part of its portfolio. EMA's legal role does not primarily comprise enabling market access. Rather the Agency's primary tasks are to protect public health and to provide scientific advice of the highest possible quality to the Community   institutions and the Member States. In view of the amount of medicinal products that are conditionally or exceptionally authorised and of the questionable timeliness of fulfilment of conditions imposed on such products, and considering several projects aiming for faster authorisations without proper measures to improve available evidence, refocussing on these goals seems necessary.

In addition, we would welcome the addition of comments concerning questions on transparency such as availability and access to data submitted by the marketing authorisation holder to the agency. Individual patient data from regulatory trials should be accessible for independent researchers.

Additionally, EMA should outline its possible role in guaranteeing market launch in all European markets, for example by implementing a "medicines tracker" to follow up if and when centrally authorised products are actually launched throughout Europe and avoid "strategic launch sequencing".

## 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 | ○ | ○ | ○ | ◉ | ○ |

1.

Biomarker endpoints are surrogate endpoints. Validation of endpoints based on biomarkers needs to be done prior to marketing authorisation and is a duty of the applicant.

Only biomarkers, that have proven to either select a subpopulation that benefits significantly more from a treatment than other patient populations or that changes in those biomarkers are directly related to clinically relevant changes in patient relevant outcomes are acceptable. Clinical development programmes and biomarker qualification need to satisfy this demand.

EMA should provide a proper description of methods for biomarker validation to be adhered by applicants.


2 and 3.

Up until now, no uniform definition of unmet medical need is available. As an entry criterion for the proposed process, a clear definition is indispensable. This definition needs to be based on a public health perspective. The integration of evidence that fulfils the needs of HTA and payers in the development programmes is very important and necessitates the development of a clear structured participation of those stakeholders. However, the question whether so-called creative payment models are fit for purpose is not within the remits of EMA

EMA needs to develop methods for an impartial and transparent participation of all stakeholders involved throughout the life cycle.

In addition, the Agency needs to develop appropriate mechanisms for reevaluation as well as withdrawing marketing authorisation when products do not live up to their expectations in the long run


3.

PRIME relies very much on the prospect of achieving a strong connection between assessors and product. Acknowledging the fact that this facilitates a better understanding of the product and possible problems arising during development, it bears the risk of bias and an inappropriate self-binding effect. Shortening the time to marketing authorisation often is connected to a greater reliance of post-marketing evidence generation, which results in a risk shift to healthcare systems. This has been widely criticised in adaptive pathways, but also is applicable for PRIME. Thus, PRIME needs to stay limited to certain specific cases and appropriate measures against institutional capture need to be implemented. It should also be examined whether PRIME is able to fulfil its goal of accelerating market access while improving available evidence. Today, this seems yet unproven. The promotion of PRIME is therefore not necessary


4-6

In view of novel manufacturing technologies, medical devices and borderline products as well as new materials we support the conception that regulatory models need to be reviewed to adapt to those products without compromising the quality of decisions. This clearly results in the need for special expertise. However, the task of protection public health urges the application of the highest standards of assessment.


7.

We want to remind of the European Ombudsman inquiry of scientific advice. Although consistent advice throughout the development is desirable, enough flexibility needs to be preserved to react to new developments and avoid inappropriate self-binding.


**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**:

8.

The 3R principles are an established but hard to implement. Their use should be further optimised, but also limits of models should be respected. As they do have their role in pre-clinical development, their value in clinical development is limited.


9.

Innovation in clinical trials is a vague concept. Up until now, many so-called modern trial designs have been discussed, but methodological problems that result in a high susceptibility for bias have not yet been solved. Thus, they need to be regarded as being acceptable for explorative trials only. Surrogate endpoints present problems that are quite similar to those discussed for biomarkers above. As long as they have not been validated for predicting patient relevant outcomes, their use for establishing a positive benefit-harm-relation cannot be recommended. One prime example is PFS, which only in selected diseases and disease status predicts OS or QoL and is used far too often – resulting in approval of medicinal products that fail to deliver benefits to patients.


10.

Before developing methodologies to incorporate big data, it should be made clear under which circumstances, for which products (pharmaceuticals in vitro diagnostics vs. Borderline products), and for which purposes this kind of data can and will be used in regulatory decisions
There should be a definition, which quality standards have to be fulfilled for the incorporation of such data into regulatory decision-making; the HMA-EMA Joint Big Data Taskforce rightly identified the need for standardisation and data quality as key prerequisite for data analyses
Additionally, questions related to data protection and data ownership need to be addressed.
However, it will be very relevant to address also potential advantages of new data sources. For example in clinical trials, the exploration of novel methods of self-measurements by patients can be supportive, as long as they represent patient relevant outcomes.


11.

The expansion of communication of the benefit-risk assessment is strongly supported. While it has to be clarified that HTA/payers and regulators have different responsibilities that should not be blended and that respective methodological standards should not converge to a minimum, understanding the reasons for regulatory decisions is key to the former. In addition, remaining uncertainties should be described in more detail than currently. Regarding patient preferences, methodological caveats have to be taken into account – preference studies are too often misleading, as preferences change with experience with illness, get imprecise with increasing complexity of decisions and tend to not elucidate the whole picture.


12. / 13.

Social and demographic changes are renewing the necessity of efforts to address special population. Nevertheless, one should take into account that the proposed adaptive approaches for iterative development result in a risk shift from pre-marketing to post-marketing. This may result in a greater population under risk instead of the intended risk minimisation. Speedy access in populations of urgent need should not be a standalone aim without taking effectiveness/efficacy and safety into account.
A supplementation of clinical trial data by clinical care date is surely valuable, but should be clearly distinguished from attempts to forego clinical trials. Modelling and simulation enhancement should not apply to ALL products. They are already encountering their limits in paediatric populations – if justified at all - and are difficult to explain in biosimilar development. Therefore, their expansion should be corroborated by striking and representative examples. It should be specified when these approaches will be used, foremost when they should replace clinical trials.

## 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**:

15.
It is highly welcomed that EMA aims for continuing its partnership with healthcare systems. Although differences exist in the way HTA and EMA examine new medicines, these differences are justified and do not hinder better cooperation. However, the differences should be better explained in the public domain.

The incorporation of evidence needed by payers and HTA into developments plans is indispensable. However, the intention of bridging from benefit-risk to relative effectiveness remains unclear. HTA and regulators have different responsibilities and therefore ask different questions. When monitoring the impact of decision-maker engagement, target parameters should be defined. While discussion often focusses on access alone, in reality, the triangle of access, affordability and added benefit is relevant.
Please also elicit what «contributing to HTA priority setting» is supposed to mean.

16.
EMA refers to an undesired fragmentation of payment models. Healthcare systems are organised on a national level and have developed differently. Therefore, the development of a single platform for interaction is supported, a unification of payment models though is undesirable and beyond the scope of a regulatory strategy.

17.
One needs to be aware of potential conflicts of interest patient representatives and patient organisations. We support the focus on patient relevant outcomes, but also remind of the fact that a common understanding with HTA and payers should be established. This is also applicable for quality-of-life questionnaires, where e. g. the often-utilised EQ5D is not preferred.

18. / 19.
Promotion of real-world data (RWD) remains a vague and questionable concept.
Firstly, RWD is better described as observational data. Using this term provides a more precise description of the underlying data and does not indicate erroneously that interventional data would be artificial and not reflecting reality.
Secondly, it is unclear, how RWD can be of relevance in a pre-authorisation setting, when no patients are treated outside of clinical trials. In a post-authorisation setting, RWD contributing to extensions of indications is viewed critical. Gathering evidence for the assessment of new indications is borderline to promotion of off-label use.
Thirdly, observational data can only provide evidence for correlation – infering from correlation to causality is yet to be solved.
Instead of promoting RWD it should be emphasized that RCTs are still the gold standard for demonstrating efficacy. RWD can provide additional information but it is more suited in the post-authorization phase. Under which circumstances and for which questions RWD can be used throughout a product's life cycle should be clarified as well. Issues are standardisation, data quality, registration in publicly accessible databases, reproducibility, validated statistical analyses and transparency on conflicts of interests of interested parties. We further ask EMA to elicit issues surrounding data protection and ownership and highlight (financial) responsibilities for data collection and putting in place infrastructure for data exchange. It will be necessary to incorporate specific reasons why and for what purposes evidence development is shifted into the post-marketing space and to also explain strategies how these data will impact on any changes in MA such as withdrawals, re-assessment.

20.
We are also aware of the need to improve product information. Neither SPC nor package leaflet are fully satisfying for the intended user. However, the concept of a real-time product information comes with several problems: Product information are legal documents, which limits their flexibility and calls for consistency.
In addition, the paper form of the package leaflet has to remain to ensure that also digitally-naïve patients can access the information provided.

21.
We share the goal of promoting availability and uptake of biosimilar medicinal products. As earlier with generics, biosimilars are an important possibility to cut costs for medicinal products without endangering

care for individual patients. Therefore, biosimilar authorisation needs to remain a high standard process and communication on this fact needs to be strengthened. In addition, it may be worthwhile to restrict applicants in their variation in devices, as this is misused to establish minor monopolies and ostensible advantages. Guidelines on the exchangeability of biosimilars would be appreciated.

22.
We also agree in the necessity to strengthen trust and confidence in the EU regulatory system, but see the need to remind of the fact, that trust is best built on reliability and transparency. The observed trend to over-utilise fast track approvals, which inherently increase uncertainties, and the seeming competition with FDA, has already unsettled several stakeholders and should not be further expanded.

## 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**:

23.

We support the aim of implementing health threat plans and refining preparedness approaches.

24. / 26.

The development of new antimicrobial agents in the view of increasing antimicrobial resistance is key for future healthcare provision. Nevertheless, we question that evidence requirements should be different to other medicinal products. Additionally, neither business models nor vaccination decisions are remits of EMA.

25.

It remains unclear, how regulatory decisions may influence the location and extent of manufacturing capacities or tackle manufacturing issues resulting in shortages. Regarding these issues, more information would be desirable.

27.

Repurposing is a promising field for further support. The development of a suitable framework to support the repurposing of medicinal products is a topic of ongoing discussions within STAMP.
Even though we in principle support the development of a framework for repurposing, we are very cautious regarding details. Importantly, we need to avoid that the repurposed drugs lead to new intellectual property rights and therefore to higher prices – also for those patients using the drug for the current disease. Otherwise, it will endanger accessibility. We have seen in the past, especially in the US, how single marketing authorisation holders exploited their monopoly on old active substances to raise prices to unaffordable measures. We have also seen marketing authorisations for old active substances in new indications based on very scarce data (literature, registries, etc.) which afterwards also asked for extremely high prices. This should be avoided, especially when the applicant has not performed most of the clinical development or when a new indication is imposed due to a proposal by a third party (learned society, healthcare provider, etc.).
The latter would also require a change in the legislative framework that could also be fit for imposition of other changes in the SPC to keep it up-to-date. It will also be challenging to learn how much information from the proposed frameworks for data collection can be used in practice, keeping in mind that quality of such observational data may be mixed and standards should not differentiate between repurposing and applications for extensions of indications according to the usual regulatory path.
In general, a better definition of EMA's role in this regard should be provided.

## 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**:

See also the comments on Strategic goal 5

28.
It is unclear whom the term «funders» refers to: national research centres, payers, or commercial parties? Health care professionals, payers and patients should be involved. Under all circumstances, transparency has to be ensured in all research collaborations.

One obvious partner for EMA is academia. Interestingly, when looking at the topics outlined (PROs, omics-based diagnostics, drug-device combinations, modelling and simulation) one important topic seems to be missing, although it has already played a major role in earlier strategic goals: Academia could also play an important role in defining novel clinical trial designs and developing methods to enable adequate analyses of data obtained.

When engaging with IMI, one needs to be aware that in a market economy, privately held companies and regulators do only partially share common goals. Conflicts between the protection of public health and maximising revenues to achieve return of investment hamper the possibilities of cooperation in public-private partnerships and increases the risks for conflicts of interest.

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