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Public consultation on EMA Regulatory Science to 2025

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Introduction

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

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

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

Completing the questionnaire

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

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

Data Protection

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

Questionnaire

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

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

Name of organisation (if applicable):

Other: Critical Path Institute's International Neonatal Consortium (INC)

About C-Path

Critical Path Institute (C-Path) is an independent, nonprofit organization established in 2005 as a public and private partnership. C-Path's mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global consortia that currently include more than 1,600 scientists from government and regulatory agencies, academia, patient organizations, disease foundations, and dozens of pharmaceutical and biotech companies. C-Path U.S. is headquartered in Tucson, Arizona and C-Path, Ltd. EU is headquartered in Dublin, Ireland, with additional staff in multiple remote locations. For more information, visit c-path.org and c-path.eu.

About INC
The International Neonatal Consortium (INC) is a global collaboration formed to forge a predictable regulatory path for evaluating the safety and effectiveness of therapies for neonates (http://c-path.org /programs/inc/). The consortium engages the global neonatal community – families, neonatal nurses, academic scientists, regulators, pharmaceutical investigators, advocacy organizations, and funders – to focus on the needs of the neonate. Launched by the Critical Path Institute, INC aims to advance regulatory science for this underserved population through teams that share data, knowledge, and expertise.

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 proposed strategy is comprehensive for innovative processes and should serve to advance regulatory science in Europe and beyond. The plan represents an expansion of EMA roles and responsibilities and would need to be adequately resourced to be successful. In addition to the focus on innovation, the strategic plan would benefit by paying more attention to improving "business as usual".

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)

12. Invest in special populations initiatives

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 number of initiatives could be undertaken to facilitate medicines development for the neonatal population, including the following:
1. Consider a range of incentives for sponsors who are developing medical products for paediatric and rare disease populations. Incentives could include patent extensions, vouchers, and other mechanisms that have been adopted in other jurisdictions and are valued by sponsors. While necessary, incentives are not sufficient.
2. In many neonatal conditions, the lack of underpinning science about mechanisms and natural history of the conditions is a significant barrier to the development of robust regulatory science. EMA, working with other regulators, could promote ways of working that are rigorous and stringent while meeting important therapeutic needs in a timely manner. For example, reliable and sensitive endpoints that accurately capture treatment benefit are unavailable for most neonatal trials. EMA could participate in consortium efforts to develop biomarkers, clinical outcome assessments, and disease progression models for neonatal trials.
3. Apply innovative methods in clinical trial design, which may reduce the burden on study participants, families and investigators.
4. It is encouraging to see Patient-Reported Outcome (PRO) measures are considered in the Strategy. The EMA and other stakeholders will need to pay particular attention to the development of "proxy PROs" (i.e. observer-reported outcome measures) that are completed on behalf of study participants who are unable to communicate their experiences, such as parents acting on behalf of neonates.

Second choice (h)

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

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.

RWD is a massive untapped resource in neonates. In Europe, eNewborn and its members are ready to contribute (See eNewborn: The Information Technology Revolution and Challenges for Neonatal Networks. Haumont D, NguyenBa C, Modi N. Neonatology. 2017;111(4):388-397). Similarly, the iNeo is positioned to contribute RWD (See http://www.ineonetwork.org). Sources of RWD need regulatory guidance and a signal that their work is valued by regulators. Guidance from regulators about acceptable approaches to collecting and analyzing RWD is likewise needed to stimulate the necessary investment by industry in RWD.

Development of the sources of RWD will be best done pre-competitively so that RWD reflects populations rather than medicines of interest to specific companies. EMA and other regulatory agencies need to work in a timely manner with pre-competitive consortia and providers of RWD to co-produce data and data standards that are fit for purpose.

Third choice (h)

28. Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science

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.

Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science: ensure that such partnerships include the other stakeholder groups that are critical to the success of the partnership, namely industry, patient advocacy groups, other non-profit and governmental organizations.

The strategic plan should mention the opportunities that will arise from working with qualified clinical research networks on the development of clinical development programmes and the execution of clinical trials. The networks are particularly strong in paediatrics in Europe (the c4c consortium) and the USA (iACT and the Duke Clinical Research Institute). The European Network of Paediatric Research at the European Medicines Agency (EnprEMA) provides a unique forum for these networks. Similar clinical research networks exist for some therapeutic areas. Developing structured approaches for these networks to contribute to the work of the regulatory network (including training, quality control of expert advice, and work towards data sharing) will enhance the EMA's current ad hoc approach to engagement with academics.

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

The proposed strategic plan is fairly comprehensive; it covers both critical elements and those initiatives that could accelerate medical product development. Additional areas that could be productively addressed are listed below.

1. One area that is not explicitly addressed is the need for EMA to align with other global regulatory agencies on clinical trial design and methods for evaluating the safety and efficacy of medical products. Particularly for rare diseases, differing requirements around the globe can significantly impede progress. Moreover, when vulnerable populations such are neonates are involved, the ethics of requiring additional trials to carry out slightly different trial designs are questionable. It will be essential to conduct clinical trials in multiple countries simultaneously in order promote efficiency, reduce costs, and accelerate drug development efforts.

2. The new systems for assessing devices (including co-development of medicines and devices) in Europe pay inadequate attention to paediatric needs. EMA needs to collaborate with device regulators to address this policy gap. This is particularly important with respect to neonates when approaches (including benefit-risk assessments) need to be tailored to the specific needs of neonates, their care-givers and families.

3. Maternal-fetal health requires more than enhanced observation of exposure to existing medicines. EMA should support the promotion of the development of medicines that will be used during pregnancy (see Medicine safety in pregnancy and ambitions for the EU medicine regulatory framework. Saint-Raymond A, de Vries CS. Clin Pharmacol Ther. 2016 Jul;100(1):21-3). As a matter of urgency, the European regulatory network needs to develop a guidance paper that mirrors the recent FDA draft guidance and reflects the needs of the community (see Challenges in Designing Clinical Trials to Test New Drugs in the Pregnant Woman and Fetus. Turner MA, Kenny L, Alfirevic Z. Clin Perinatol. 2019 Jun;46(2):399-416).
EMA needs to support other stakeholders to develop appropriate incentives for the formal development of medicines used in pregnancy, and to remove unnecessary barriers to research during pregnancy such as misconceptions about the ethics of research in pregnant women.
The enormous progress made in “mainstreaming” research about paediatric medicines needs to be reproduced with respect to research during pregnancy.

4. Supply problems are not limited to novel products (3.4.3). Neonates may be vulnerable because of the small market size and relatively few options. On the other hand, when appropriate formulations are available in some jurisdictions it can be difficult to move them across borders. See “Product Substitution as a Way Forward in Avoiding Potentially Harmful Excipients in Neonates. Nellis G, Metsvaht T, Varendi H, Lass J, Duncan J, Nunn AJ, Turner MA, Lutsar I. Paediatr Drugs. 2016 Jun;18(3):221-30. Product substitution involving the most frequently used products containing potentially toxic excipients may spare almost half of neonates from unnecessary exposure to these excipients. Close collaboration of all stakeholders is required to resolve the technical and logistical issues surrounding practical achievement of product substitution.

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:

#3 Investing in PRIME is critical for developing therapies for neonates, which is an area of great unmet need. EMA could leverage existing collaborations with families, academia, and sponsors to shorten timelines , ensure optimal trial design, and facilitate global integration and collaboration. PRIME could be further enhanced through incentives such as extension of market exclusivity for neonatal and rare paediatric diseases.

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**:

#12 Investing in special populations initiatives is critical to advancing therapies for these populations. Likewise, innovation in clinical trials (#9) is very important for developing neonatal therapies. The investigator, family and regulatory communities need to accept that innovative methods may be risky in the sense that they don't give information that contributes directly to medicines development even if the methods are attractive in terms of reduced burden on study participants.

It is encouraging to see that PROs are considered in the Strategy. The EMA and other stakeholders will need to pay particular attention to the development of "proxy PROs" that are completed on behalf of study participants who are unable to communicate their experiences, such as parents acting on behalf of neonates.

In many neonatal conditions the lack of underpinning science about mechanisms and natural history of the conditions is a significant barrier to the development of robust regulatory science. EMA, working with other regulators, needs to promote ways of working that are rigorous and stringent while meeting important therapeutic needs in a timely manner.

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**:

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

RWD is a massive untapped resource in neonates. In Europe, eNewborn and its members are ready to contribute but need regulatory guidance and a signal that their work is valued by regulators. (See eNewborn: The Information Technology Revolution and Challenges for Neonatal Networks. Haumont D, NguyenBa C, Modi N. Neonatology. 2017;111(4):388-397).

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**:

#24 With the rising rate of antibiotic resistance, it is very important to support efforts at developing new antimicrobial strategies and working with other governments to implement antibiotic stewardship programs. Sepsis occurs in one to eight per 1,000 live births with the highest incidences occurring among preterm infants. An arsenal of effective antibiotics is needed to treat affected infants.

#27 Support the development and implementation of a repurposing framework

Repurposing is attractive to special populations, particularly neonates. EMA can explore ways to support expedited development specific to neonates using multiple sources of data tailored to the specific gaps such as extrapolation; formulations; benefit-risk assessment using a range of sources, including RWD. RWD is likely to be particularly useful in neonatal repurposing because many medicines used off-label in neonates can be repurposed from other indications.
EMA should work with other stakeholders to improve the incentives for repurposing and the development of off-patent medicines.

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

	Very important	Important	Moderately important	Less important	Not important
28. Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science	◉	○	○	○	○
29. Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions	◉	○	○	○	○
30. Identify and enable access to the best expertise across Europe and internationally	○	◉	○	○	○
31. Disseminate and share knowledge, expertise and innovation across the regulatory network and to its stakeholders	○	◉	○	○	○

Please feel free to comment on any of the above core recommendations or their underlying actions. **Kindly indicate the number of the recommendation you are commenting on**:

#28 is very important yet not complete. The collaborations needed for advancing regulatory science go well beyond tapping the academic community to undertake studies such as the natural history of a disease. To adequately capture disease progression, patient input is required to identify what symptoms are of most importance to persons living with a disease and experts in measurement science are needed to develop robust methods of measuring treatment benefit. Also fundamental to collaborations that advance regulatory science are those that are global. EMA resources could be more effectively leveraged through active participation in global consortia.

The strategic plan should mention the opportunities that will arise from working with qualified clinical research networks on the development of clinical development programmes and the execution of clinical trials. The networks are particularly strong in paediatrics in Europe (the c4c consortium) and the USA (I-ACT for Children and the Duke Clinical Research Institute). The European Network of Paediatric Research at the European Medicines Agency (EnprEMA) provides a unique forum for these networks. Similar clinical research networks exist for some therapeutic areas. Developing structured approaches for these networks to contribute to the work of the regulatory network (including training, quality control of expert advice, and work towards data sharing) will enhance the EMA's current "scattergun" approach to engagement with academics.

#29 is closely related and should be integrated into #28

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