Public consultation on EMA Regulatory Science to 2025

> Fields marked with * are mandatory.

* Name

* Email

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):

Critical Path Institute Huntington's Disease Regulatory Science Consortium (HD-RSC)

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.

The Huntington's Disease Regulatory Science Consortium (HD-RSC) is a collaboration formed by C-Path and CHDI Foundation, Inc. with the aim of creating new tools and methods to advance efficient clinical development and address the regulatory needs for approval of Huntington's disease (HD) therapeutics. The HD-RSC currently comprises representatives from pharmaceutical, biotechnology, and technology companies, and from numerous academic institutions and non-profit biomedical research and advocacy organizations; when appropriate, the HD-RSC also seeks to coordinate with both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) to identify expectations for implementation of tools and solutions developed by the consortium. Overall goals are to accelerate HD therapeutic development and inform clinical trial design by building disease-progression models and clinical-simulation platforms, as well as coordinating the identification of reliable biomarkers and the development of clinically meaningful outcome measures across the disease continuum.

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 HD-RSC has reviewed the strategic goals and core recommendations and wants to applaud the EMA for their consideration of novel approaches and the identification of opportunities for innovation in regulatory science across the industry. The strategy proposed in EMA's Regulatory Science to 2025 document is comprehensive and outlines recommendations across human health initiatives. The EMA has considered aspects of medicine and health that are meaningful now and in the future. Implementation of these recommendations will have significant impact for stakeholders across the industry and will drive innovation throughout phases of clinical development.

Drug development in HD faces many challenges that are captured in the core recommendations. We identify, in order of importance, core recommendations #9 (Foster Innovation in Clinical Trials), #1 (Support developments in precision medicine, biomarkers and 'omics'), and #3 (Promote and invest in the Priority Medicines scheme (PRIME)) as strategies leading to the greatest impact in HD. We believe that combined implementation of these three core recommendations will support therapeutic development to bring safe and effective therapies to the HD community. Nonetheless, there are several other recommendations that we perceive as important to the HD community.

Core recommendations supporting the translation of gene-based therapies from bench to bedside will also have significant impact to HD drug development. Current treatment paradigms in clinical study for HD include intrathecal delivery of gene-therapy products (antisense oligonucleotides, or ASOs), as well as direct injection of viral vectors containing therapeutics directly into deep brain structures. Other therapeutic approaches continue to advance in all stages of pre-clinical development, including more traditional modalities such as small molecule discovery and lead optimization. Some of these stated approaches, however, will not be sustainable without innovation in the supply and manufacturing of these classes of drugs. Successful delivery of these therapies to patients will require collaboration with payers in order for these expensive therapeutics to be affordable and accessible.

In addition, progressing the regulatory framework to support advancements and implementations of digital technology will greatly impact the HD field. Digital technologies, including the use of wearable technology for real-world data generation and app-based clinical assessments administered remotely, are already being implemented in HD clinical studies. The growing trend towards incorporating this data for decision making highlights the need for the regulatory systems to have the infrastructure in place to utilize this data in the review process. As new approaches emerge, it will also be necessary to encourage interaction between sponsors and academic developers early and often to understand the utility and optimize the capabilities of digital technology.

Furthermore, as therapeutics advance that aim to modify the progression of HD, optimization of modelling and simulation capabilities will be critical to better inform drug development and ensure that we deliver the right drug, to the right patient, at the right time during their disease progression. Investments in modelling and simulation will assist several other EMA core recommendations, including to "foster innovation in clinical trials," incorporate "artificial intelligence in decision-making," promote the "use of high-quality real-world data in decision making," "engage with big data," and "support developments in precision medicine" to deliver patient and disease-stage specific therapeutics.

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

Strategic goal 1: Catalysing the integration of science and technology in medicines development (h)
- ⦿ Yes
- ○ No

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

- ◉ Yes
- ○ No

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

- ◉ Yes
- ○ No

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

- ◉ Yes
- ○ No

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

- ◉ Yes
- ○ No

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

First choice(h)

9. Foster innovation in clinical trials

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

- The proposed underlying actions to foster innovation in clinical trials will significantly impact HD drug development over the next five years. We support the immediate implementation of these actions and encourage the Agency to continue to identify and seek feedback for areas of innovation in HD and other rare genetic diseases. These diseases represent areas of high unmet medical need and are also high-risk programs for sponsors. Clinical trial design in these diseases is challenging, as rare diseases often have an incomplete understanding of disease progression and trial size is typically limited. HD therapeutic development is affected by all of this and would benefit from innovation and risk-taking in clinical trial design and implementation. Additionally, opportunities to "integrate the provision of regulatory advice along the development continuum" to support alignment on the clinical value of new and emerging endpoints, and to continue to encourage the adoption of novel practices and collaborative initiatives would be valuable.

- New endpoints are currently being developed in the HD community to support stage-specific intervention and will need critical assessment to facilitate their use. This is especially important for very early treatment of HD, which has not yet been feasible. Assessing the clinical relevance and value of these endpoints and biomarkers will enable clinical trials throughout all stages of HD. Important endpoints are emerging in the digital data space. Digital data provides opportunities for continuous and potentially more sensitive read-outs. They offer the potential to detect clinical efficacy of a therapeutic more rapidly than relying on scheduled clinician visits. Traditional endpoints in HD rely on subjective clinician-reported assessments that introduce variability into both the baseline value as well as the endpoint. Objectively-measured digital endpoints may reduce variability in clinical trials as well as provide additional relevant data. For HD drug development, it would be of great interest to develop a regulatory framework for utilization of digital measures in clinical trials and create a path to approval that would be supported by these novel measures.

- We would like to promote the broader use of "capabilities in modelling and simulation and extrapolation" to support innovation in clinical trials, especially in rare diseases such as HD. It is important to note that these modeling and simulation platforms rely on support for data sharing initiatives to aggregate clinical trial data with real world, natural history, and/or observational study data for interrogation. Use of clinical trial simulation platforms should be encouraged to optimize clinical trial design and to inform enrichment and effect size by integrating placebo effects, disease progression, and drug/disease interactions. In HD, the expansion length of the CAG repeat explains some, but not all, of the variability in disease onset and progression. Modelling and simulation tools would help understand additional sources of variability in order to define homogenous patient populations for inclusion in clinical trials. As HD is a rare disease with a rapidly developing landscape of emerging therapeutics, the ability to identify more precisely targeted clinical trial candidates, utilize adaptive or alternative trial designs, and reduce the need for large placebo groups will greatly assist HD drug development.

- Overall, there are many opportunities to foster innovation in clinical trials, all of which will benefit patients by leading to more efficiency in the drug development and regulatory processes.

Second choice (h)

1. Support developments in precision medicine, biomarkers and 'omics'

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.

• Novel biomarkers are urgently needed to optimize treatment timing, inform patient enrollment, monitor progression, and assess the impact and efficacy of medications on the health of the patient. Regulatory guidance on the potential utility of new biomarkers under development for use in HD clinical programs, as well as legacy biomarkers, is needed to inform further biomarker development and translate treatments from animal models and pre-clinical studies to clinical trials. Alignment on biomarkers in HD will be critical to enable early treatments that are safe and effective. Utilization of biomarkers to evaluate a treatment's impact on clinical outcomes will enable early treatment of HD and reduce clinical trial duration.

• 'Omics' work is very important to advancing HD drug development. While the responsible gene has been identified and genetic testing is now available, understanding additional genetic, epigenetic, and other factors' impact on the course of HD would promote the understanding of disease pathogenesis and support the delivery of targeted and precision medicine to this population.

• In addition to the actions proposed, we also perceive intersection between the "developments in precision medicine, biomarkers and 'omics'" with the "translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments." The translation of novel therapeutics, such as gene-based therapies currently under development for HD, into effective treatments is dependent on a robust measure of biological change linked to long-term clinical benefit.

• Finally, we propose that "developments in precision medicine, biomarkers and 'omics'" should be integrated with "modelling and simulation" initiatives. Biomarkers and genetic variants can be considered as covariates in disease progression and drug-disease models to help understand and reduce variability in clinical trials as well as correlate biomarker changes with long term benefit.

Third choice (h)

3. Promote and invest in the Priority Medicines scheme (PRIME)

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.

• The actions proposed for the investment in PRIME are critically important to sponsors seeking drug approvals for HD. Therapies in the development pipeline could provide major therapeutic advantages over currently approved treatments targeting motor symptoms. Investment in the Priority Medicines scheme will encourage the regulatory framework to rapidly bring novel and urgently needed therapeutics to HD patients. This will also provide additional incentive and support for sponsors to pursue high-risk clinical programs in rare diseases such as HD. Early interactions and more diverse communication with regulators would allow for the integration of more frequent regulatory advice to shorten the duration of the development process. It would also benefit the HD community to have specific guidance on adaptive trial design in rare diseases to enable accelerated approval.

• Several additional core recommendations also relate to the successful implementation of the PRIME scheme, including the generation and "use of high quality real-world data (RWD) in decision making" to support post-approval. We also perceive that post-approval frameworks could be supported by "capabilities in modelling and simulation and extrapolation." Investment in PRIME will enable the development of the regulatory framework to effectively and efficiently support the above-mentioned areas, leading to the greatest impact to patients by bringing novel therapeutics from bench to bedside in a shorter period of time.

• Finally, public-private partnerships such as the HD-RSC are another component of the communication and collaboration proposed. Such consortia are well-positioned to provide an outlet for regulators to give advice to large groups of stakeholders in a single setting.

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

We note two elements missing in this strategy that we believe are significant. First, there is a critical need to encourage data sharing across the industry. Actions related to this include continuing support for clinical trial data transparency, implementing requirements for the use of study data standards, such as CDISC standards, in new submissions to improve data quality, facilitate review, and promote interoperability of clinical data and research, and establishing guidelines for informed consent form language to enable sharing of patient-level data with biomedical research organizations and public-private partnerships. Second, there is a need to support development of rehabilitation therapies to support treatment options for advanced or late-stage patients who will not be eligible to receive or cannot afford novel treatments when they become available.

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:

#6: This recommendation is of particular significance in the neurosciences. As new technologies and therapeutics emerge, we would like to see investment of efforts to advance our ability to cross the blood-brain barrier and facilitate the delivery of much-needed therapies directly into the brain.

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**:

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**:

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: A common cause of death in Huntington's patients is due to complications from pneumonia. Advancing efforts to support development of new antimicrobials and alternatives would address this problem and thus be of great interest to the HD community.

#27: Repurposing frameworks will also play an instrumental role in future treatment programs, as late-stage patients will not qualify for treatments targeting early disease stages and will need symptom management as they progress.

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**:

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

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