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Public consultation on EMA Regulatory Science to 2025

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Introduction

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

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

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

Completing the questionnaire

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

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

Data Protection

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

Questionnaire

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

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

Please specify: Press/media/NGO/Not-for profit organisation/other scientific organisations/policy maker, etc.

The Critical Path Institute (C-Path) is an independent non-profit 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.

Name of organisation (if applicable):

Critical Path Institute Ltd.

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.

C-Path appreciates the opportunity to provide feedback on EMA's Regulatory Science to 2025 strategy. Overall, C-Path finds EMA's strategic plan to advance regulatory science to be appropriately ambitious in its desired impact on the field. The strategic vision incorporates the full spectrum of medicine discovery, development, and ultimate delivery to patients. The strategic vision emphasizes the need for translational science to turn basic scientific research into regulatory science solutions that impact all aspects of drug development. While the vision is broad in scope, the detailed mechanisms for EMA to facilitate the execution of the strategic vision are somewhat lacking. Future publications and initiatives that support the overall strategic vision should include more details on the implementation of each aspect of the strategic plan.

Several important themes recur throughout the report that will underpin the success of the strategic vision. These foundational aspects are echoed in each core recommendations and must be thoughtfully executed. For example, the need for broad collaborative efforts that allow for the sharing of knowledge, resources, and risks. The importance of these efforts cannot be over stated or over simplified. C-Path's experience and ability to convene a diverse group of stakeholders, often with competing individual interests, to work together towards a shared vision has been significantly refined over time. C-Path has been successful in realizing the power of these consolidated collaborative efforts and would urge EMA to continue to expand its support of public-private partnerships (PPPs) and consortia-based programs. The work achieved through PPPs is made publicly available to maximize the benefits of its work. Stakeholder consensus allows a field to move faster and farther than an individual entity is able to. Precompetitive PPPs also provide a means for regulatory agencies to engage with stakeholders to align the work with regulatory thinking. In this paradigm, scientific research is focused on the regulatory processes of developing new medicines, which is often an afterthought without input from regulators. When successful, the benefits are felt by researchers, drug developers, regulators, and patients, with therapeutic areas that have lacked the interest of developers becoming revitalized. Further, the setbacks of inevitable failures are shared, and thus, the overall impact is minimized. PPPs and consortia allow for the execution of the collaborative efforts found throughout the

strategic vision, and are the catalyst to innovation across drug development.

Another important component of many strategic goals is the identification and sharing of data to answer important regulatory science questions. Regulatory agencies must continue to encourage collaborative access to data through meaningful data sharing efforts. No unmet need in regulatory science can be met without the availability of robust data to support proposed solutions. Individual datasets are often insufficient to support cutting-edge science and technology into the complex process of drug development. Thus, data must be integrated from many sources if new tools are to meet regulatory science needs. In today's climate where most are champions of data collaboration, too few will meaningfully share data. EMA initiatives that lower the barriers to data sharing are imperative, and EMA must continue to play a leading role in pioneering mechanism to overcome these barriers. EMA must also continue to protect patient privacy, while encouraging data sharing to occur.

Advances in modeling and simulation have the potential to make broad impact across regulatory science, but are only as applicable as the data that underpins a model will allow. The broader the availability of data, the broader an extrapolation can be made. The advent of artificial intelligence and machine learning holds great potential across regulatory science, but will rely on the availability of large databases. Similarly, datasets that reflect patient experiences in real-world settings are invaluable to advancing care for the public. These data can be used throughout a product's lifecycle, including post-approval safety monitoring. Safety signals may only be seen in large integrated databases from many sources. The ability to monitor for emerging health threats across Europe will require multi-national efforts and mechanisms that allow individual local databases to communicate with other similar databases.

Overall, for most strategic goals to be meaningfully accomplished, data and knowledge sharing between stakeholders is fundamental. Accordingly, C-Path would recommend intense focus on advancing data sharing initiatives, as is discussed throughout the strategic plan.

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

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

- (●) Yes
- ( ) No

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

- (●) Yes
- ( ) No

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

- (●) Yes
- ( ) No

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

- (●) Yes

- ○ No

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

- ◉ Yes
- ○ No

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

First choice(h)

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

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

The potential for real-world data (RWD) to make drastic advances in regulatory science is high, if mechanisms that turn RWD into real world evidence (RWE) can be realized. There are two broad categories of RWD: RWD that already exists, i.e. retrospective RWD and RWD that will be collected in the future, i.e. prospective RWD. Both will be important in unlocking the full potential of RWD.

Retrospective RWD exists in the form of electronic health records, medical claims databases, patient or product registries, and other sources that were often not collected with the goal of answering regulatory medicine development questions. Thus, existing RWD is often 'messy' and requires significant curation to be capable of informing regulatory decision-making. However, the sheer volume of data in these databases could yield incredible insight that would dramatically affect patients' lives. Electronic health records and medical claims databases offer extremely large existing data bases that could be leveraged to generate meaningful evidence regarding the usage of medicinal products. When coupled with advances in artificial intelligence (AI) and machine learning, data can be meaningfully extracted from these data sources to generate evidence throughout a product's lifecycle. However, given the limitations of these databases, particularly the inherent heterogeneity, quality control concerns, and issues of patient privacy, a framework for the incorporation of retrospective RWD in regulatory decision-making must be thoughtfully considered. The development of novel means to answer important questions regarding the quality of RWD, and therefore its ability to generate quality RWE, is essential. Further, guidance documents from regulatory agencies directing stakeholders who engage in this task will facilitate the generation of RWE from retrospective RWD, and should be emphasized.

While many limitations of retrospective RWD can be avoided with prospective RWD, important questions remain. For example, how will multiple structured sources of RWD be standardized to aid in regulatory decision-making? How will RWD be deemed fit-for-use in a specific regulatory context? Initiatives to collect prospective RWD must therefore be thoughtfully crafted and designed with the regulatory context and relevant data standards in mind. The advent and near universal availability of digital measures that capture and generate RWD, the potential for pragmatic or virtual clinical trial design, and the design of patient, disease, or product registries intended to answer regulatory questions all have potential to dramatically change the process of drug development, if appropriately cultivated and developed. Again, further refinement of existing guidance documents and regulatory framework, with particular emphasis on the importance of data standards in the collection of prospective RWD, will allow prospective sources of RWD to deliver robust evidence to expand access to new medicines and improve care for patients.

Further, the development of novel methodologies for medicine development can be significantly impacted by RWD. Novel methodologies lead to the identification of important biomarkers, clinical outcomes assessments, and advances in precision medicine that affect whole therapeutic areas. Robust development of these tools catalyze development by reducing risk and streamlining medicine development programs. Novel methodologies for drug development that include RWD can inform safety monitoring, patient selection criteria, trial design considerations, and endpoint selection. In rare diseases, RWD can facilitate the development of decentralized or geographically distributed clinical trials. C-Path has experience leveraging real-world patient registry data towards the development of novel methodologies and multiple ongoing current efforts. C-Path's Polycystic Kidney Disease Outcomes Consortium incorporated RWD from multiple sources to support the use of total kidney volume (TKV) as a prognostic biomarker for use in clinical trials of patients with autosomal dominant polycystic kidney disease. In a 2015 Qualification Opinion, CHMP supported the use of TKV in clinical trials and stated the effort was foreseen to help optimize the development of clinical trials.

The overall potential for retrospective and prospective RWD to impact broad swaths of regulatory science and drug development make this core recommendation extremely valuable in the Regulatory Science to 2025 strategic vision.

Second choice (h)

13. Optimise capabilities in modelling and simulation and extrapolation

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.

As stated in the strategic reflections document, the use of modeling and simulation (MS) can improve the efficiency of medicines development by reducing the need for, and improving the design of, preclinical and clinical studies. C-Path believes the uses of MS in drug development are far reaching. Thus, investing in initiatives that advance and optimize capabilities and applications of modelling and simulation into the medicine development regulatory science space will be amplified by enabling topics discussed in other core recommendations, such as exploiting digital technologies and AI, and will potentiate many other core recommendations, such as fostering innovation in clinical trials, developing regulatory framework for emerging digital clinical data generation, supporting the development and implementation of a repurposing framework, and an ability to better leverage novel non-clinical models and replacement, reduction, and refinement (3R) approaches.

C-Path has significant experience and expertise in the use of MS to develop novel methodologies for use in drug development. For example, work led by C-Path in Alzheimer's disease (AD) led to the development of a novel disease progression and trial evaluation model that was deemed suitable for qualification by CHMP in 2013. This model has since been used to aid in the design of clinical trials of mild and moderate AD. C-Path's work to develop another model-based enrichment tool for patients with amnestic mild cognitive impairment resulted in a letter of support from EMA, which stated "…this model will allow sponsors to optimize clinical trial design, perform power and sample size calculations, inform entry criteria, define enrichment strategies, define stratification approaches, and determine the operating characteristics of the different simulated studies." C-Path applauds EMA for its ongoing recognition of the value found in MS techniques and would encourage EMA to continue prioritizing the advancement of these tools.

Advanced MS allow for complex dynamics to be mathematically modeled and tangibly understood. This, coupled with an understanding of a dataset's limitations and uncertainty, provide solid grounding to inform regulatory decisions throughout the medicine development process. Identification of potential new active substances, dose selection for human trials, prediction of safety or efficacy signals in clinical trials or post-approval surveillance, and extrapolation of safety and efficacy to new populations are all enhanced through MS. Further, complex and adaptive trial designs are made possible through MS. The totality of impact from the application of MS throughout a product's lifecycle results in safer and more efficacious medicines available to patients sooner.

The ability for MS to drive innovation throughout regulatory science is compounded by its ability to facilitate advances in other important aspects of the strategic reflection. For example, to effectively carry out the 3Rs strategy to replace, reduce, and refine animal testing, other means must be able to assess the effects and toxicity of new compounds prior to testing in human subjects. Similarly, according to strategic goal #9: Foster innovation in clinical trials, "innovation may come through the use of novel trial designs, endpoints, or techniques for gather data, or the use of new techniques such as 'omics' to stratify populations or disease taxonomy." Each aspect listed is enhanced with modeling techniques. For instance, clinical trial simulation tools enable adaptive clinical trial designs, disease progression models can facilitate identification and assessment of multiple potential endpoints, especially surrogate endpoints, by incorporating the complex interactions of multiple disease components into one model. Clinical trials entry criteria can be better informed by modeling the interaction of relevant patient baseline features with clinically meaningful outcomes to identify patients likely respond to novel therapies.

Finally, as advances in MS, including machine learning and AI, continue, EMA must provide guidance for the inclusion of advanced models into drug development. EMA must also effectively educate industry and academic stakeholders engaged in MS for drug development to ensure tools are developed according to the standards set by EMA. For efficient uptake of MS throughout regulatory science, adequate exchange of knowledge must exist between those advancing basic modeling techniques, those developing models for use in medicine development, and regulators who both use and assess relevant models. Further, broad use of these models will require educational initiatives, like those ongoing at C-Path, that teach those without modeling expertise the value of MS in drug development.

Third choice (h)

1. Support developments in precision medicine, biomarkers and ‘omics’

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.

Precision medicine can be defined as the goal of advancing care by considering individual variability in biology, environment, and lifestyle. When successful, precision medicine facilitates researchers and medicine developers' ability to identify and develop medicines more likely to work in a particular patient population, often leading to more efficient drug development processes. To patients, this translates to safer, more effective. At its core, all precision medicine efforts fundamentally rely upon biomarkers and 'omics-based markers to inform patient and population level decisions about novel and existing medicinal products. These tools inform every aspect of medicine development, including preclinical and clinical safety monitoring, patient stratification and clinical trial enrichment, and the identification and development of surrogate endpoints that facilitate more efficient clinical trials. Developments in precision medicine, biomarkers, and 'omics will underpin and greatly affect many other Strategic Goals and Core Recommendations within the overall strategic vision, making this a highly important core recommendation.

For example, translation of advanced therapy medicinal products (ATMPs) from benchtop to bedside requires appropriate and adequate means to assess their safety and efficacy in patient populations. Biomarkers, 'omics, and other efforts to enhance precision medicine are fundamental to understanding how ATMPs, which often utilize cutting-edge first of its kind technology, will affect patients. ATMPs have the potential to treat or cure devasting diseases, but also have potential for significant unintended and untoward adverse effects. Important questions remain for monitoring the toxicities of ATMPs, and developing biomarkers or 'omics specific to cell and gene therapies is crucial for their ultimate success. Similarly, significant questions remain regarding the safety of nanotechnologies in drug development. Smart materials can adapt to their environment in predictable ways, but identifying and monitoring biologic response, positive and adverse, will require the discovery and development of new biomarkers. Non-clinical models and simulations can incorporate various biomarkers to help broadly understand disease progression and to inform clinical trial design. Thus, to ensure these regulatory science initiatives are effectively pursued, furthering the development of biomarkers and 'omics to inform their development must be prioritized.

Overall, innovation in clinical trials and precision medicine is catalyzed through robust identification and development of novel biomarkers. For example, better informed patient entry criteria, endpoint selectin, and safety monitoring are all facilitated through better biomarkers. Similarly, genomics, proteomics, and metabolomics have been incorporated into nearly every facet of medicine development, however the lack of data standards in these areas poses a significant challenge to maximize their potential utility and impact in regulatory science. As these tools fully mature, EMA must keep pace with scientific advances by continuing to emphasize and expand their focus on advancing precision medicine through the development of advances in biomarker and other 'omics-based technology.

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

Most notably, the specific role of consortia and not-for-profit organizations is absent. While there is emphasis on the value and importance of broad collaborative efforts, specific support for consortia and other public-private partnerships (PPPs) will add value to any regulatory science effort. Consortia and PPPs, such as those managed by C-Path, offer a neutral pre-competitive space for organizations with competing or conflicting interests to work together towards a common goal. This facilitates meaningful collaboration between pharmaceutical industry, academic researchers, healthcare professionals, patient advocates, and regulators. Collaborations take the form of data sharing, contribution of resources or expertise, consensus-building dialogue, and ultimately the development of new standards and tools that advance a therapeutic area and regulatory science. The willingness of individual organizations to work towards a common goal is amplified when the convening group is a trusted, experienced, knowledgeable, and neutral third party. C-Path has 15 years of success as this type of organization and a robust history of regulatory science

deliverables that have shaped regulatory science innovation. C-Path firmly believes the Regulatory Science to 2025 effort would be significantly strengthened by adding emphasis to the role of consortia throughout regulatory science.

The importance of data-sharing in advancing regulatory science has been discussed, but cannot be understated. While data-sharing and data-pooling are referenced multiple times in the report, there is little focus on lowering or removing barriers to data sharing. In C-Path's experience, while most encourage the concept of data-sharing, too few will meaningfully share data. The perceived barriers or restrictions cited as prohibitive are often easily reconciled through established processes. C-Path's data contribution agreement (DCA) process has been refined throughout its history, has overcome nearly every barrier to the data-sharing process. Most perceived barriers have ready solutions. For example, DCAs explicitly state acceptable uses and disclosures of shared data and how data will be secured. DCAs are legal documents that govern all aspects of the data sharing process and can eliminate the most frequently cited concerns of unpublished data being scooped, used against a sponsor's interest, or intellectual property concerns. The ability to only view a data in a portal is insufficient to support new tools for use in the regulatory space. Data must be shared with regulators so due diligence analyses can be performed. A clear and consolidated effort to break down barriers to meaningful data sharing must be developed. Efforts to protect patient privacy must also incorporated into data sharing efforts. Allowing patients to have a stronger voice in the use of their data may advance data sharing and alleviate many privacy concerns. Future Regulatory Science to 2025 reports, and the work it aims to advance, would be best served with the addition of a specific initiative that would turn data sharing champions into data-sharers.

The overall strategic vision would also be enhanced with focus on novel methodologies for drug development. Much of the existing strategy falls under the heading of novel methodologies or are significantly impacted by novel methodologies. Biomarker and 'omics that advance precision medicine, advances in modeling to enhance clinical trial design, and non-clinical models to inform early development could all be considered novel methodologies. Further, the development of ATMPs, innovation in clinical trials, initiatives in special populations, and other core recommendations would be enhanced through novel methodologies. Direct consideration for the development of novel methodologies would further increase the likelihood of success of the overall initiative.

Finally, as discussed above, detailed information regarding the implementation and execution of the strategic vision are lacking, including a clearly articulated processes for EMA to carry out the strategic vision. It is important to clearly inform the public and relevant stakeholders who wish to join EMA in its efforts on the mechanisms for their involvement. Collaboration is inherent to each strategic goal, however, details are absent as to how these collaborations can engage with EMA. C-Path, which has been granted SME status, would encourage EMA to continue to support SME enterprises and EMA should encourage PPPs, consortia, and other organizations to increase their presence in Europe by continuing to offer benefits to SME enterprises. PPPs, consortia, and other collaborations that work to meet regulatory science needs are only successful when regulatory authorities are intimately involved. Clear mechanisms for stakeholders to engage with and include EMA in their efforts should be considered in future publications.

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:

Core Recommendation #2: Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments
•Advancing manufacturing practices is fundamentally important to ATMPs. Manufacturing is currently a major rate limiting step in the development of gene therapies which has resulted in delayed starts for clinical trials or clinical trials being halted because of concerns in the manufacturing process. For these therapies to advance, attention must be given to manufacturing processes.
•Many, if not most, rare diseases will likely leverage ATMPs as novel therapies are developed, and thus special consideration should be given to rare disease as pathways for regulatory endorsement of ATMPs are refined.
•Longitudinal safety analyses are also important. At FDA, the Center for Biologics Evaluation and Research (CBER) requests up to 15-years of follow up safety data for certain products that would be considered ATMPs. C-Path would urge EMA to consider how the safety, especially the long-term safety, of ATMPs will be assessed and monitored.

Core Recommendation #3: Promote and invest in the Priority Medicines scheme (PRIME)
•An important aspect for the continued success of the PRIME scheme is the determination of products that eligible for PRIME designation. Current schema focuses on “medicines that offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options.” Better understanding on what constitutes “major therapeutic advantage” would be helpful in identify new medicines that may be eligible for PRIME.

Core Recommendation #6: Develop understanding of and regulatory response to nanotechnology and new materials’ utilisation in pharmaceuticals
•Similar to the discussion above of ATMPs, advancing manufacturing excellence and appropriate monitoring for short- and long-term safety are important.

Core Recommendation #7: Diversify and integrate the provision of regulatory advice along the development continuum
•Public-private partnerships and consortia offer acceptable and appropriate mechanisms for regulatory agencies to provide guidance while avoiding concerns of bias or favoritism towards an individual company or product. As discussed above, these groups offer a precompetitive space that allow for learning to benefit whole communities, rather than one organization. The voice of the regulator is powerful and important in guiding regulatory science initiatives. Public workshops, publications, and participation in public-private partnerships or consortia allow this voice to be heard in a neutral setting to shape innovation in regulatory science and therapeutic areas.

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**:

Core Recommendation #9
•Innovation in clinical trials will be seen through the advancement of other key aspects in regulatory science. In particular, advances in modeling and simulation and the development of precision medicine, biomarkers, and the various 'omics disciplines is important. Innovation can be driven through modeling and simulations that allows for classic trial designs to be more efficient, and adaptive and complex trials designs to be possible. The development of biomarkers allows for better informed inclusion criteria, endpoint selection, and monitoring of safety and efficacy. Further, biomarkers can be included in models and simulations to further advance the utility of both.
•One important component of innovative clinical trials is the betterment of endpoints and the identification of surrogate endpoints that allow for shorter duration trials to provide meaningful insight into long term outcomes. Questions remain as to how surrogate endpoints should be adequately validated in order to be used in clinical trials. EMA could consider publication of evidentiary considerations for the development of surrogate endpoint markers.
•Administrative processes must also be streamlined for innovation in clinical trials to be realized. For example, the process for amendments to ongoing clinical trials is long and arduous. Innovative trials designs may be of short enough length that delays to protocol amendments due to administrative processes could significantly impact the ability of the innovative trial design to add efficiency into the overall medicine development process.

Core Recommendation #10
•Important questions remain for the implementation of emerging digital health technologies in regulatory science. Consideration must be given for how digital measures can add value to medicine evaluation. Digital health technologies have the potential to provide more sensitive measures of disease processes, but this may not always be valuable information. For example, wearable devices worn on the wrist may offer greater insight into tremor associated with many diseases. A more sensitive measure of tremor will not be more informative than existing measures in patients with fulminant disease. However, more sensitive measurements may allow for earlier detection of tremor before fulminant disease occurs. In this scenario,

therapeutic intervention may be initiated earlier than would be without the use of the digital technology. A clear framework for how digital measures can provide meaningful insight into medicine development is key. Digital devices can also generate extremely large data sets. Thus, important consideration must be given for the interpretation and analysis of this data.

Core Recommendation #12
•Special populations often lack significant clinical trial data sources to support important regulatory decisions. Thus, reliance on RWD in these populations is key. Similarly, modeling and simulations can be key to investigate the utility of existing drugs in special populations, while mitigating the risk of exposing these patients to medicines thus far untested in that population. Physiology Based Pharmacokinetic (PBPK) modeling can allow for better drug exposure hypotheses and reduce the number of patients needed for adequate PK studies. In rare disease populations with small patient populations, disease progression models can make it possible to assess the overall effect of a drug on the disease, even with few patients. They can also facilitate master protocols and other novel clinical trial designs that enhance the feasibility of controlled trials is small populations.
•An important consideration to invest in special population initiatives is financial support for broad efforts focused on special populations. Pharmaceutical industry partners must be incentivized to devote resources to therapeutic areas that represent either high risk or low return on investment. Public-private partnerships and consortia offer effective mechanism to consolidate resources to advance efforts towards particular special populations, but must find adequate funding to support their work. EMA supported programs to fund these efforts will have significant impact on patients in special populations.

Core Recommendation #14
•The creation of a dedicated AI test “laboratory” would facilitate the development of a framework for the use of AI in regulatory decision-making. AI is poised to make significant impact in all aspects of healthcare, but must be done so with appropriate caution. AI is still a relatively young field, and while it promises much innovation, its implementation must be carefully assessed. Efforts to allow external expertise on AI to collaborate with regulatory scientists at EMA should be prioritized to ensure the regulatory utility of AI is commensurate with its true capabilities. Further, guidance documents should be published to inform the appropriate use of AI in drug development.

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**:

Overall, alignment between HTAs and EMA will serve to benefit patients by increasing efficiency and reducing the burden on medicine developers. While HTAs are most interested in data that reflects real world use of medicines, regulators are often concerned most with determining if a medicine is safe and efficacious for use in the general public. Advancing the utility of RWD in regulatory decision-making promises to bring increased alignment between these goals, which will reduce the need to generate two sets of data. Further, open communication and transparency is key in considerations for decisions that may support both marketing authorization and payment and reimbursement.

Core Recommendation #17: Reinforce patient relevance in evidence generation
•The patient voice in the development of evidence for new medicines allows the perspective of the end-user of a new product to be included in the regulatory decisions of that product. Broadly, this can include patient measures that support safety and efficacy or measures that reflect patient preference. Both aspects should be considered important. Further, patients and their advocates should be engaged starting early in the development of a new medicine.

Core Recommendation #19: Develop network competence and specialist collaborations to engage with big data
•"Big data" is likely best leveraged through innovation in machine learning and AI. However, there are significant barriers to including these techniques into regulatory decision-making. Thus, networks created to establish means for big data to be included in regulatory decision-making must include experts in machine learning and AI.

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**:

Core recommendation #26: Support innovative approaches to the development and post-authorisation monitoring of vaccines
•The incorporation of RWD surveillance efforts into efforts that would provide increases in approaches in post-authorisation monitoring of vaccinations. Large, multi-national systems, such as VigiBase are fundamentally important. Better RWD platforms, potentially linked to electronic health records, would promote this core recommendation.

Core Recommendation #27: Support the development and implementation of a repurposing framework
•As previously discussed, retrospective and prospective RWD offer immense potential to allow for repurposing of medicines that are already available to patients. However, for this data to be effectively put to use, a proper regulatory framework must exist to effectively manage the concerns surrounding the use of RWD and to provide sponsors with appropriate direction for the inclusion of RWD in regulatory submissions. It is important to find meaningful mechanisms to incentivize sponsors to pursue label expansions, and also to allow non-profit organizations, who are unable to promote the use of any specific product, to be able to engage in efforts aimed at repurposing medicines to expand their acceptable use.

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**:

Overall, Strategic goal five is lacking inclusion of non-academic based partners who engage in fundamental research to advance important areas in regulatory science. Consortia and public-private partnerships can and do have vast impact in medicine development and regulatory science. When regulatory agencies participate in these groups, their impact is magnified. Thus, as collaborative efforts between regulators and important stakeholders are developed to identify strategic regulatory science areas, advance and develop potential solutions, and communicate the findings, knowledge, and experience of the group, C-Path would urge EMA to include consortia and public-private partnerships.

Core Recommendation #28: Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science
•The inclusion of consortia and public-private partnerships who represent the voices of pharmaceutical industry, academic researchers, health care practitioners, patients, and often regulatory agencies, must be included in partnerships to identify important needs in regulatory science. Consortia and public-private partnership provide the mechanisms for all stakeholders to find consensus on important topics and to share resources in developing solutions. Calls to establish research collaborations can be amplified by leveraging

relevant collaborations that already exist. Thus, the partnerships developed to advance this strategic goal must go beyond academia and include a broader swath of stakeholders. Also important in these conversations is the voice of industry, who must also champion innovative solutions if they are to be incorporated into medicine development programs.

Core Recommendation #29: Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions
•Similarly, leveraging existing collaborative efforts provides a means to rapidly address emerging problems and to pool resources to identify and develop solutions. The ring-fencing of EMA resources to address rapidly emerging regulatory science questions by directly investing in solutions or in groups working to develop solutions is an important aspect of this goal.
•Expanding and developing new regulatory science education initiatives to train the next generation of regulatory science researchers and further develop current regulatory scientists is fundamental. Regulatory Science fellowship programs and graduate level Regulatory Science didactic coursework through partnerships with universities and regulatory agencies, like those ongoing efforts of C-Path, allow early career scientists to transition their skills into the regulatory science realm. Similarly, C-Path is currently developing training modules on the utility of model informed drug development initiatives throughout regulatory science. The goal of these modules is to educate those without technical modeling expertise on the value of modeling and simulation in order to increase the usage of these tools in the development and review of novel agents. Similar targeted training modules made broadly available to regulators, researchers, and developers will ensure that cutting edge technology and techniques are meaningfully and broadly incorporated into the processes of developing new medicines. Overall, C-Path believes investment in training future regulatory scientists has limitless return for the field.

Core Recommendation #30: Identify and enable access to the best expertise across Europe and internationally
•A knowledge management system should be considered and developed in order to ensure the knowledge and expertise of the experts who work with EMA is retained. Harmonization between all facets of EMA that engage with external experts will be important to have one unified system to capture and leverage the work done with external experts.

Core Recommendation #31: Disseminate and share knowledge, expertise and innovation across the regulatory network and to its stakeholders
•It is important to clearly define what is meant by “open exchange of knowledge”. As previously stated, in today’s climate, many champion the concept of sharing of data, but far less actively engage in meaningful data-sharing. Multi-stakeholder partnerships allow large numbers of organizations to work together, but the success of these efforts is fundamentally reliant on a willingness to share and exchange knowledge openly. Initiatives to clearly define, support, and instruct knowledge holders on how their knowledge can be meaningfully shared should be a high priority for EMA.

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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