Fostering interactions in regulatory science

RSNN's Response to Public Consultation on EMA Regulatory Science to 2025

The European Medicines Agency (EMA) drafted a proposed strategy on Regulatory Science to 2025. A public consultation on this strategy was set up to seek views from EMA's stakeholders, partners and the general public and to investigate if it meets stakeholders' needs. This document describes the views of the Regulatory Science Network Netherlands (RSNN) on the Human part of EMA's proposed strategy.

RSNN'S OVERALL VIEW ON PROPOSED STRATEGY

EMA has prepared a comprehensive and ambitious strategic plan to anticipate on and prepare for the regulatory challenges ahead of us. We consider that the strategic plan foresees in significant contributions to innovating and improving regulatory aspects affecting the entire product life-cycle and its sub domains (quality, non-clinical, clinical and pharmacovigilance), societal and stakeholder interaction, and will also provide opportunities for operational optimisation of the European regulatory system by making use of emerging technologies (e.g. big data and AI, imaging, biomarkers, B/R quantification, patient-preference elicitation, etc.).

However, exchange and use of scientific information with all stakeholders is currently underdeveloped in the current draft. We consider it essential for the success of the overall strategy to foster interactions and stimulate participation to contribute to the strategic programme by all stakeholders engaging in regulatory science, including in the development of the plans on how to reach the goals set out in EMA's strategic document. The challenges set out in the strategic document are ones we need to tackle with society as a whole to realize the potential that is contained within this strategic document.

CORE RECOMMENDATIONS

Below, in order of importance, we discuss the top three recommendations in EMA's strategic document of which we believe they will deliver the most significant change in the regulatory system over the next five years.

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

Public private partnerships offer a unique opportunity to research regulatory challenges from all possible viewpoints in order to arrive at regulatory recommendations. Further synergy can be achieved when all stakeholders have equal seats at the table, as is the case in RSNN. The prerequisite for these interactions is that all regulatory discussions take place in the precompetitive space. RSNN is a network of experts from industry, academia, regulatory authorities, and the broader regulatory science field. RSNN offers a unique platform for stakeholders from different backgrounds to meet and discuss regulatory science as equal partners.

Our mission is to advance an efficient and effective regulatory system that supports medicines development, marketing authorization, access, and appropriate use of medicines. RSNN shares and disseminates knowledge among all stakeholders and sets the agenda for further research (see e.g. our newsletter on innovating the SmPC; https://webtools.lygature.org/wp-content/uploads/2018/09/201805-RSNN_Nieuwsbrief5_A4_v0.5-MR_e-mail.pdf). The initiative was started by the Medicines Evaluation Board (MEB) and the Association Innovative Medicines. Its secretariat and organization are supported by Lygature, which previously managed the TI Pharma Escher programme. (Gispen-de Wied and Leufkens 2013).

We recommend a similar approach in the EMA strategic document in order to include all (scientific) partners to contribute to the challenges that have been set. Furthermore, it is important to clearly define in this document who is identified as a partner for scientific engagement from the outset: as an editorial comment, we would propose to reword goal 28 as follows: 'Develop network-led partnerships with academia and other (scientific) partners to undertake fundamental research in strategic areas of regulatory science'.

Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions

Within Europe, there are already networks in place engaging in regulatory science. Notably, and excluding our own network, these include the Centre for Innovation in Regulatory Science (CIRS), a UK based subsidiary of Clarivate Analytics, formerly the IP & Science business of Thomson Reuters), the Copenhagen Centre for Regulatory Science at Copenhagen University (CORS) and the European Federation for Pharmaceutical Sciences (EUFEPS) regulatory science network. We highly recommend making use of the existing networks that already have an established track record in engaging in regulatory science in order to fully leverage the potential for research and regulatory innovation.

The strategic document should also outline what will be achieved as a result of the collaborative efforts. Finally, it is not clear what constitutes a network scientist and we recommend this to be as inclusive as possible.

Disseminate and share knowledge, expertise and innovation across the regulatory network and to its stakeholders

Acceptance and adoption of novel regulatory science and its consequences by all stakeholders requires intensive sharing and dissemination of knowledge. This requires a form of integrated knowledge translation to close the gap between science and practice (Graham et al. 2009). The same holds true for regulatory science. To fully realise the vision of EMA set out in the strategic plan, a comprehensive and dedicated approach to share data across the network is recommended and should include deliverables. Multi-stakeholder regulatory science networks, like the RSNN or CORS, could be a powerful platform for these activities.

SIGNIFICANT MISSING ELEMENTS

The RSNN believes two significant elements are missing from EMA's strategic document. First, EMA definition of regulatory science is focussed on informing regulatory decision making throughout the lifecycle of a medicine and contributes to the development of regulatory standards and tools. This is closely aligned to the definition used by the FDA (Hamburg 2011). However, this definition is limited in scope since it excludes research of the regulatory system itself (Schellekens, Moors and Leufkens 2011). We therefore propose that regulatory science is the science of developing and validating new standards and tools to evaluate and assess the benefit/risk of medicinal products, facilitating sound and transparent regulatory decision making, and also advancing knowledge of regulatory systems in general, via analysis of the frameworks used and of their effectiveness; does the system deliver what society expects and asks for? By including this crucial aspect of regulatory science, deliverables and rethinking of strategic goals can be further shaped. We underwrite the need for a high-level document describing the strategy for the way forward. But this can only be reached by a subsequent detailed description on how this should be reached. It should be explicitly encouraged that all stakeholders should participate (Leufkens 2019). This should start at the onset of further developing EMA strategic document and include the formulation of research questions, the research, analysis and dissemination of the knowledge.

Second, while the strategic goals are virtually all output driven, what is missing is a reflection on the development and methodological strengthening of regulatory science itself. Indeed, our first remark drives this point home even further: there is, to date, no

consensus on the definition of our chosen field of research. In order to fully capitalize on the outcome of the research programme that is being proposed, it is necessary to also focus on developing the methodology of regulatory science (e.g. Jonker et al. 2018). Every science needs an array of agreed upon principles, such as defining the research question, which theory to apply, which study design to choose or develop, how data sources are accessed and how data is extracted from them, how the analysis was performed, etc.

REFERENCES

- CC Gispen de Wied and HG Leufkens. From molecule to market access: drug regulatory science as an upcoming discipline. Eur J Pharmacol. 2013 5;719(1-3):9-15. doi: 10.1016/j.ejphar.2013.07.021.
- H. Schellekens, EHM Moors, HG Leufkens. Drug Regulatory Systems Must Foster Innovation. Science 2011: Vol. 332,6026, pp. 174-175. DOI: 10.1126/science.332.6026.174
- ID Graham, J. Tetroe, M. Gagnon. Lost in Translation: Just Lost or Beginning to Find Our Way? Annals of emergency Medicine Vol 54; Issue 2, 2009. pp. 313-314.
- Jonker CJ, Kwa MSG, van den Berg HM, Hoes AW, Mol PGM. Drug Registries and Approval of Drugs: Promises, Placebo, or a Real Success? Clinical Therapeutics. 2018 May;40(5):768-773. DOI: 10.1016/j.clinthera.2018.04.005
- Leufkens HG. Regulatory science: Regulation is too important to leave it to the regulators. Br J Clin Pharmacol. 2019 Apr 10. DOI: 10.1111/bcp.13917
- MA. Hamburg. Advancing Regulatory Science. Science 2011: Vol. 331, 6020, pp. 987. DOI: 10.1126/science. 1204432