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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:***

between 1 and 1 choices

- [x] Individual company
- [ ] Trade association
- [ ] SME

Name of organisation (if applicable):

Novo Nordisk A/S

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.

Novo Nordisk welcomes the opportunity to offer comments on the Agency's Regulatory Science Strategy to 2025 (hereafter referred to as RSS 2025). Within these comments, Novo Nordisk identifies priorities that we believe will have the most substantive benefit for European citizens, as well for the global community, by ensuring that Europe remains at the frontier of innovation in healthcare. Novo Nordisk
Novo Nordisk is a global healthcare company with more than 95 years of innovation and leadership in diabetes care and other chronic diseases. Every day about 30 million patients use our products. Novo Nordisk is headquartered Denmark and has more than 20,000 employees in Europe.

Novo Nordisk supports the responses submitted by EFPIA and EuropaBio. Our response is based on the EFPIA response and supports the same 3 priority goals:

Rec 2.2 Foster innovation in clinical trials
Rec 1.7 Diversify and integrate the provision of regulatory advice along the development continuum
Rec 3.4 Promote use of high-quality real-world data (RWD) in decision-making

In addition, we want to emphasize the importance of the following goals:

Rec 1.1 Support developments in precision medicine, biomarkers and 'omics
Rec 1.2 Support translation of advanced therapy medicinal products (ATMPs) into patient treatments
Rec 1.4 Facilitate the implementation of novel manufacturing technologies.

In determining the final RSS 2025, EMA will need to balance the requirements to deliver near-term process improvements with long-term strategic direction for delivering meaningful change Novo Nordisk encourages the EU regulatory system to continue its focus on facilitating the navigation across Committees and national agencies who assess a candidate medicine at different stages of development.
Novo Nordisk's Input to Prioritise and Deliver the Regulatory Science Strategy to 2025: All five strategic goals within RSS 2025 address important priorities for the advancement of medicines and therapeutic care in Europe. In many cases, the recommendations set out by EMA are interrelated and interdependent. Some recommendations are clearly enablers of others, and therefore, the order in which these recommendations are progressed is likely to be critical to their success. Following EMA's reflections from this consultation, industry anticipate the release of EMA's 5-year implementation work plan, which will detail the Agency's

priority operations to action its regulatory science strategy.

Additionally Important Recommendations:
Novo Nordisk's top three priorities listed above address the most urgent recommendations to bring innovative new treatments to European patients. Along with these priorities, Novo Nordisk wishes to emphasise the RSS 2025 recommendation to Support developments in precision medicines, biomarkers and 'omics' (Rec. 1.1) with a view to advance the concept of personalised healthcare.
Novo Nordisk also highlights the recommendations to Facilitate the implementation of novel development and manufacturing technologies (Rec. 1.4). Manufacturing of medicines is evolving to embrace new models such as continuous manufacturing and stakeholders should further collaborate to advance these approaches. Optimising Capabilities in Modelling, Simulation and Extrapolation (Rec. 2.6) is very important. Currently, at times, EU regulators seem hesitant to accept alternative approaches to the provision of evidence generated by modelling, simulation and extrapolation during development, as well pre- and post-initial authorisation. Increasing acceptance of predictive approaches, based on modelling and simulation (M&S/MID3) and extrapolation will advance the clinical development of medicines (e.g., within paediatrics and geriatrics). In addition, acceptance of models for non-clinical, CMC and Quality factors will also add value. Furthermore, Rec 1.2 Support translation of advanced therapy medicinal products (ATMPs) into patient treatments is important for EU to keep up with the pace in this area.
Moreover, Novo Nordisk recognises the importance of addressing better coordination in the provision of advice between regulatory authorities and HTA bodies. EMA has undertaken considerable efforts to bridge the coordination gaps between decision makers, and there have been some gains achieved. However, in order to deliver a step-change in consistent, aligned decision-making for the benefit of patients, it will require a refreshed approach (including greater involvement of patients and healthcare professionals), recognizing that regulatory, HTA and reimbursement processes and decisions are separate and occur at different stages of development.
Novo Nordisk would value the continuation of the EMA's stakeholder engagement, including the full participation of HMA/NCAs, frequent status updates and outreach technology platform meetings, throughout the 5-year implementation phase of the RSS 2025 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)

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.

Novo Nordisk's highest prioritised RSS 2025 recommendation is Foster innovation in clinical trials (Rec 2.2) as we believe it has the potential to deliver the most significant impact in the regulatory system over the next five years. Data generated through clinical trials (CTs) is the foundation of drug development and the use of complex CTs (CCTs) is becoming more established. EMA's prioritisation of this topic would support further advancement of future and innovative clinical trial concepts (e.g., adaptive seamless design, trials in small populations, extrapolation) which will be instrumental in bringing novel medicines to patients earlier. Efforts on this topic, should also provide an opportunity to modify some of the current inflexibilities in the provision of scientific advice and regulatory approval system for CT applications. Importantly, this topic also encompasses some of the other priorities, which relate to new clinical evidence sources (e.g., registries, RWD, Big Data), outcome measures (e.g., PROs. endpoint, biomarkers), and methodologies (e.g., M&S). Indeed, the field of innovative CTs is evolving rapidly including the value of novel (e.g., digital) endpoints. Fully benefiting from these advances will not be possible without cohesive progress on the supportive recommendations from the RSS 2025 listed below.

Supporting Recommendations:

- Support developments in precision medicine, biomarkers and 'omics (Rec 1.1)
- Develop the regulatory framework for emerging clinical data generation (Rec 3.3)
- Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products (Rec 1.5)
- Reinforce patient relevance in evidence generation (Rec 3.3)

Key Proposed Actions:

- Implement a new CCTs strategic initiative. To align with industry's innovation efforts for drug development, Novo Nordisk strongly encourages the Agency to develop a new strategic initiative to broaden the use and acceptability of complex innovative clinical trials based on experiences so far and with the support of all relevant stakeholders and experts (e.g., medicine developers, patients, clinicians, regulators, ethics committees, and HTA bodies). To best achieve this ambitious recommendation, the following additional actions are proposed.
- Organisation of dedicated multi-stakeholder collaborations (e.g., workshops, demonstration projects and pilot schemes) to raise awareness, share case studies and learnings, and identify best practices. The

Agency has previously hosted a number of successful workshops, including with industry, to progress important topics such as M&S, dose-finding studies, and paediatric extrapolation. CCTs workshops would facilitate the use and acceptability of innovative tools and methods to be used in drug development. The workshops could incorporate learnings from IMI projects and could focus on key challenges around CCTs design and practicalities of collaborative (multi-sponsor) clinical trials. These workshops could also include global regulators (e.g., FDA, PMDA, Health Canada).

- Facilitate better alignment between EU regulators and stakeholders in the clinical trial pathway such as the national agencies and HTA bodies. A forum should help resolve alignment issues across National Competent Authorities, ethics committees, HTA bodies and patients' organisations when considering acceptance of CCTs.
- Develop further the CT Information System (CTIS) to best accommodate CCTs. The CTIS needs to be able to efficiently accommodate managing applications for and the datasets arising from CCTs.
- Advance global coordination on the topic. Important additional CCTs topics should be proposed to ICH for better global alignment on development approaches. For example, ICH has agreed to deliberate soon on the CCT concept of 'Adaptive Designs' and additional elements of CCTs could be opportune for advancement under the ICH infrastructure.
- Develop guideline for Patient Reported Outcome Development of PRO in Europe is very uncertain and only in few cases are data allowed in the product label.
- Develop guideline for Biomarkers qualification The industry could benefit from an EU guideline
- Advance acceptance of digital endpoints. As part of the development of a regulatory framework for emerging clinical data generation, a platform to achieve multi-stakeholder input on proposed digital endpoints should be developed. One current option is the qualification opinion/advice, however this is a lengthy process that is not adapted to the agility sponsors need when deciding on a CT design. Note: also linked to "Develop the regulatory framework for emerging clinical data generation" (Rec 3.3)

Second choice (h)

7. Diversify and integrate the provision of regulatory advice along the development continuum

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.

Whilst EMA seeks to better connect the different decision-making steps across the lifecycle of a medicine, there is a similar need to better link and integrate medicine development advice across the EU regulatory ecosystem. Providing enhanced advice options with greater flexibility in the delivery of this advice is needed to reflect the changing pace and process of innovation along the development continuum, and to adaptably accommodate special perspectives for certain types of products (e.g. ATMPs, paediatrics, drug-device combination products). Moreover, this broadening and integration of regulatory advice should progress beyond EMA programmes (e.g., PRIME) to better bridge the advice and decision-making gap across the EU regulatory system (i.e., EMA, EMA's Committees, National Competent Authorities), ensure engagement from specialised EMA working group/parties, and progress beyond EU (e.g., US FDA

The overall value of pan-EU scientific advice is undermined when different and possibly contradictory opinions emerge during the development of a product. This can be through the different Committees within the EMA, but also, via the Member-State-led approach to decision-making for clinical trials. This national approach to clinical trials and the EU centralised approach to the provision of scientific advice also mean that there is no unified "line of sight" on the progress of a product during its development from early clinical trials through to approval. This contrasts unfavourably with the U.S. IND system where the FDA offers comprehensive guidance. Consequently, today, companies must attempt to weave together advice given at multiple points along drug development.

Whilst many questions to the EMA Scientific Advice are related to the clinical program, it is important that robust advice can be obtained for novel manufacturing technologies which may be implemented pre-approval or as part of Life-cycle Management. It is important that appropriate advice can be sought both early (e.g. for ATMPs) or post-approval as exemplified with novel manufacturing processes. In general, it is important that robust advice can be achieved for CMC topics e.g. use of AI.

Supporting Recommendations:

- Reinforce patient relevance in evidence generation (Rec. 3.3)
- Contribute to HTA's preparedness and downstream decision making for innovative medicines (Rec 3.1)
- Promote and invest in the PRIME scheme (Rec 1.3)
- Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products (Rec 1.5)
- Facilitate the implementation of novel manufacturing technologies (Rec 1.4)

Key Proposed Actions:

- Redesign of a more flexible and integrated R&D product support mechanism, providing agile dynamic advice across the lifecycle of the medicine. Research and development timelines are becoming increasingly efficient and should be matched by the timelier provision of advice. For example, waiting around 4-6 months from the scientific advice request to the meeting with SAWP to occur is not compatible with an expeditious clinical development programme. Novo Nordisk would welcome a quicker, voluntary, and flexible engagement with regulators and other stakeholders. The developer should have the ability to select from multiple levels of advice engagement based on the attributes of a particular product.
- Integrate the opportunity for iterative CMC data submission during review. This proposal can be achieved by delegation of advice and review of dossiers by relevant Working Parties (e.g. BWP for biologics, MSWP for M&S, Biostats WG).
- Enhance the coordination of advice across EMA Committees, National Competent Authorities and other pertinent stakeholders. Ensure closer alignment of understanding between EMA and national regulators to minimise any conflict in views between centralised scientific advice and CTA assessment.

- Provide preliminary feedback ahead of discussion meeting so that the sponsor can also suggest additional topics for discussion based on this feedback. In this way, the developer's discussion topics can be added to those determined by the SAWP/HTA bodies (i.e., a more interactive engagement process between the sponsor and the SAWP).

- Ensure wider stakeholder involvement in specific aspects of advice (e.g., CTFG for clinical trials, Notified Bodies for device/drug products)

- Within advice continuum, consider special perspectives for different types of products (e.g., ATMPs, paediatrics, drug-device combination products)
- Optimise usage of CT information System. Consider how the data to be included in the CT Information System implementation can be better used across the EU Medicines Regulator Network so that national regulators have that full harmonised insight into the clinical data generated on a product during its development even when the clinical studies on the product are not being performed in that Member State.

Third choice (h)

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

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.

In the RSS 2025, the EMA anticipates the use of high quality RWD as complementary evidence, which may be used in decision-making. To be able to expand the applicability of RWD, medicine stakeholders must also advance novel sources (e.g., digital) for gathering RWD, methodologies necessary to ensure quality and usefulness of the data, novel analytical techniques (e.g., AI, modelling), and ultimately the implementation of global standards. Understandably, these are goals which have also been recommended in the HMA-EMA Big Data Taskforce Summary Report.

As in the Task Force report, the RSS 2025 highlights the importance not only of the technical means to use RWD effectively, but also the governance and societal changes that need to accompany these efforts. Acceptability builds from experience, best practice sharing and familiarity, which suggests a key role for demonstration projects across stakeholders in EU. Piloted approaches are also ongoing in other countries and regions, and EMA should remain active in this field of research internationally. Enhanced acceptability of RWD to support regulatory decisions must also involve and evolve with patients, HTA bodies, healthcare professionals and other collaborators.

Supporting Recommendations:

- Develop network competence and specialist collaborations to engage with big data (Rec. 3.4)
- Contribute to HTA's preparedness and downstream decision making for innovative medicines (Rec 3.1)
- Reinforce patient relevance in evidence generation (Rec 3.3)
- Exploit digital technology and artificial intelligence in decision making (Rec 2.7)
- Foster innovation in clinical trials (Rec 2.2)

Key Proposed Actions:

- Launch a strategic initiative to integrate RWE in drug development, including the use of demonstrator projects to engender familiarity. This initiative should assimilate building blocks across the commonly available regulatory tools (e.g., guidance, pilots, capability building, stakeholder engagements):
  - Development of a framework with guidance on what factors should be considered and addressed in a regulatory submission to encourage exploration by industry of alternative approaches to evidence generation.
  - A dedicated EMA RWE pilot program in which regulators and sponsors can publicly share lessons learned (with protections for confidential commercial information) for the benefit of all stakeholders, which will improve the quality of RWE submissions in the future (note: further suggestions for public workshops below).
  - Continuing education resources to enhance reviewers' consistent understanding of novel RWD source types, RWD quality considerations, and evolving analytical methodologies for generating RWE (especially methods applied to observational data).
- Build on ongoing efforts (in EU and internationally) to provide clarity on scope and quality of sources of RWE, recognising governance and resources required for these sources and identifying where gaps exist. The EMA and HMA could also partner with the European Commission to develop a unified approach on the collection, curation and interoperability of health data and establishment of a European health data resource base for the benefit of European citizens.
- Seek to align and contribute to extend the standards and methodologies for collecting, analysing and validating RWE use internationally. This should also incorporate the current recommendations under consultation in the Discussion Paper "Use of patient disease registries for regulatory purposes – methodological and operational considerations". To ensure "high quality" RWD, internationally aligned fit-for-purpose quality requirements for regulatory purposes are essential. Beyond standards, however, this discipline also needs quality management in practices related to creating and using RWE sources. Establishing best practice in quality management will also need pilots to advance practice. This could include both retrospective studies, as well as prospective case studies. The methodologies must enable EMA to

trust RWE without having to re-do the analyses themselves.

• Coordinate workshops to progress dialogue and publish workshop conclusions. The impact of healthcare RWE is system-wide. To move this innovative agenda forward, regulators, industry and other stakeholders need to engage widely to help establish momentum for appropriate use of RWE. Workshops are one mechanism that has worked in other domains for regulatory change and could be used for this purpose. These workshops would be used to advance standards and best practices, build consensus and, encourage engagement across stakeholders. Furthermore case examples can be presented by industry and regulators

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

Novo Nordisk wishes to comment on the international regulatory science cooperation (page 55, RSS 2025). Novo Nordisk fully supports EMA's strong international engagement in regulatory science and harmonisation in particular in ICH.

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:

Scientific advances and new technologies are changing the understanding of diseases and enabling the development of personalised medicines. To support the development of new medicines, the EU regulatory framework serves a variety of platforms, procedures and processes at European and national level.
Novo Nordisk shares the vision that sees the Agency at the crossroads between science and healthcare and support the EMA's objective to catalyse integration of scientific innovation (e.g., 'omics', ATMPs), medtech innovation (e.g., medical devices, in vitro diagnostics) and technical innovation (e.g., additive manufacturing). The recommendations under RSS 2025 Strategic Goal 1 capture key areas through which effective regulation can translate excellent science into available care. Novo Nordisk has focused its input on the following priorities:

Very Important:

- Diversify and integrate the provision of regulatory advice along the development continuum (Rec. 1.7); One of Novo Nordisk's Top Priorities see answer to Question 5 – second choice
- Support developments in precision medicine, biomarkers and 'omics (Rec. 1.1); As precision medicine is leveraging new diagnostics/diagnostic methods, moving the regulatory science focus from treatment of disease to prediction and prevention of disease or their relapse, is of utmost importance. There is an opportunity to substantially evolve the EMA's biomarker validation process in order to encourage greater uptake and use. Further, the value of new markers is not always evaluated in the same way by HTA bodies, leading to delay in patient access to innovative personalised medicines.

- Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments For these novel technologies it is important that the EMA stays current and issues and updates guidelines which should address principles and not be overly prescriptive
- Facilitate the implementation of novel manufacturing technologies (Rec. 1.4); As highlighted in earlier in Novo Nordisk's comments, manufacturing of medicines is evolving to embrace new models such as use of AI. Dialogue between Industry and regulators on technical adaptation of the current regulatory framework is ongoing at the EMA and ICH level. A more flexible and continuous mechanism of advice is desired which will allow specialised experts in the EU Network to understand more deeply the end-to-end process and innovative multivariate analysis that guarantee the product quality. Implementation of the new technology is expected to occur both pre-approval and post-approval. Further, it would be beneficial to have a clear regulatory pathway for technology changes affecting a platform of products or sites, rather than just one dossier.

Important:
- Promote and invest in the PRIME scheme (Rec. 1.3);

Certainly, Novo Nordisk considers the PRIME scheme as an especially promising approach to bringing new products to patients for unmet medical need as early as possible. We believe that there are opportunities to further optimise implementation of PRIME. The PRIME scheme needs to allow for participation of all applicants from an early stage of development (i.e., at proof of principle stage) and should be applicable for the extension of indication, based on the same criteria as for an initial first indication. Recent trend data demonstrate that EMA's product review timelines are getting longer, and indeed, are notably longer compared with US
It is essential to review the performance of the scheme after 3 and 5 years, to ensure that it delivers the expected impact on public health (i.e. faster priority medicines to market). Proposed action to 'Leverage collaboration with patients, healthcare professionals, academia, and international partners' is seen as very important. Novo Nordisk concurs that involvement of HTA bodies in PRIME is key to ensure the generation of data along the development lifecycle to satisfy the needs of downstream decision makers on access.
Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products (Rec. 1.5); Novo Nordisk supports the proposal to create an integrated evaluation pathway for medicines that are developed and used in combination with companion diagnostics. Indeed, expertise needs to be enriched to enable adequate risk/benefit assessment of such products. In parallel of developing this evaluation pathway, it is essential for the developer to have the possibility to gain acceptance of their development plan before it is implemented. It should therefore be possible to ask for development advice from the stakeholders involved in the assessment of these products. By design, this platform should allow for timely joint advice, involving notified bodies, NCAs and/or EMA, depending on the type of questions.

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**:

This strategic goal is particularly appropriate in order to address a fast changing and important area of medicines development, and as a consequence, patients' timely access to innovative medicines. Over the last 5-10 years, there have been significant breakthroughs in medicines. While the pipeline of new medicines is also promising, today, many major diseases remain inadequately treated. Innovation is challenging traditional medicine development and regulatory practices. As such, there is a need for Europe to demonstrate that it welcomes novel approaches to data generation such as through new evidentiary sources and standards. This should, not only help optimise data collection for the benefit of patients, but also, promote Europe's competitiveness. Drug development, which should be viewed as a continuum, requires an adaptive, flexible mindset and multi-stakeholder collaboration in Europe among the Member States and beyond. The recommendations under RSS 2025 Strategic Goal 2 reflect the shared vision of improving the quality of evidence developed, and the analytical methods for integrating this evidence to support decision making.

Novo Nordisk anticipates that progress on some of the ongoing topics (e.g., paediatrics) will be maintained, and wish to provide support where appropriate. As part of this critical priority, Novo Nordisk's focus is on the following recommendations, all considered as inextricably linked to the complex or innovative clinical trial design recommendation. Indeed, fostering innovation in clinical trials necessitates the development of a regulatory framework for the acceptance of new tools and methods including the use of digital technologies. Finally, in addition to developing best practices there is the need to optimise expertise and capabilities and strengthen interactions with experts and among all the relevant stakeholders. Hence, the focus on the following recommendations which would also benefit from greater international harmonisation:

Very Important:

- Foster innovation in clinical trials (Rec. 2.2)- Top Priority: Refer to Q5 response – first choice

Important:

- Develop the regulatory framework for emerging clinical data generation (Rec. 2.3); With the rapid progress in information technology, it is essential that the necessary infrastructure to collect and store large amount of health data in digital format be further developed. Since clinical investigators and sponsors of medicine development can increasingly access data relating to health status of the populations in routine

healthcare and even home settings, industry should be a key collaborator in implementing this recommendation.

• Optimise capabilities in modelling, simulation and extrapolation (Rec. 2.6); For example, predictive and modelled approaches to safety evaluation (for active substances, impurities and manufacturing intermediates) that minimise animal utilisation is a current field of interest that demands further investment and acceptance (e.g., the EMA Reflection Paper on Qualification approaches for non-mutagenic impurities). In addition, the CMC and Quality fields are a rich source of scientific and innovative approaches using M&S and prediction that could be utilised. Examples include: use of stability modelling and prediction of degradation (for shelf-life setting and product and packaging selection),which can help take CMC development off the critical path to submission and enable early patient access and support post approval changes and innovation; PK modelling to support bioequivalence evaluation (beyond the BCS scope of the ICH M9 guideline) and dissolution specification setting; process modelling (e.g. development of a digital twin) of a manufacturing process (drug substance and/or drug product) to support development and scale up, and control strategy development.

• Invest in special populations initiatives (Rec. 2.5); EMA is encouraged to strengthen its current efforts to support drug development for special populations and improve patients' early access through appropriate research. For these patients with often a high unmet medical need, whether children, during pregnancy or the elderly, it is crucial to optimise drug development knowing that new tools and methods (e.g., M&S, RWD, use of wearables, registries) could help generate data from these patients where feasibility of standard randomised CTs is known to be challenging.

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**:

RSS 2025 Strategic Goal 3 aims to advance patient-centred access to medicines which Novo Nordisk strongly support. We recognise the need to improve timely access to valued and needed treatments for patients, and regulatory review is a foundational step in that process. Although access is often frustrated at later decision stages in pricing and reimbursement, maintaining and enhancing effective regulatory procedures must continue to be goal for EMA.

While there are a great number of initiatives to enhance patient engagement during development and regulatory processes, the methods and practices by which to incorporate patient insights into regulatory decisions is still unresolved. For example, the ability to incorporate patient reported outcomes (PROs) in clinical trials and then to include the results in labelling has not been applied consistently. The optimal involvement and connection to other important medicine stakeholders is also evolving. There are numerous examples of a lack of market access even upon regulatory approval, and enhanced stakeholder engagement should support improvements.

Key priorities and why: Very Important:

- Promote use of high-quality real-world data (RWD) in decision making (Rec. 3.4); Novo Nordisk's third highest priority - Refer to Q5 response

Important:

- Develop network competence and specialist collaborations to engage with big data (Rec. 3.5); Closely linked with Recommendation 3.4 on RWD, Novo Nordisk recognize the need for concomitant investment in the skills and networks to undertake analytical work with Big Data to support regulatory decision-making. This priority has also been identified in the HMA-EMA Big Data Taskforce Summary Report.

- Contribute to HTA's preparedness and downstream decision making for innovative medicines (Rec. 3.1); For some years now, EMA has engaged more directly with HTA bodies and has encouraged joint advice procedures for medicine developers. This effort has certainly delivered progress and fostered a better mutual understanding of evidentiary standards, methods and assessment, whilst "respecting the remit and perspectives of all sides." (p. 22, RSS 2025). There is still much to be done, particularly in balancing the challenges of matching a global development programme with a variety of local healthcare system needs.
- Reinforce patient relevance in evidence generation (Rec. 3.3); Novo Nordisk welcomes the EMA's past efforts to provide patients with a substantive role in the regulatory process in Europe, which has certainly

informed better decision making and provided patient insights earlier in the development pathway. The big step to take now is on how to include patients more directly in the definition and collection of the evidence itself, which also links to the recommendation 3.4 on RWD.

• Deliver improved product information in electronic format (ePI) (Rec. 3.6); There is important work already underway to progress the ePI agenda by the EMA and HMA, with opportunities to reach key milestones in the near term. Novo Nordisk sees this as a longer term strong patient centric effort and supports this.

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**:

Strategic Goal 4 to address emerging health threats and availability/therapeutic challenges is a core responsibility of a regulatory authority, and as such, it is clear that this agenda must remain part of any strategy for improvement. The recommendations included capture a number of factors that are recognised societal priorities for current health needs and which Novo Nordisk strongly supports (e.g., AMR, vaccines and supply challenges). As such, we have provided comments, based on its remit, only on those recommendations considered "Important" above.

The question arises to what extent these essential goals are exceptional projects rather than "business as

usual" and may, in some cases, extend beyond the boundaries of Europe and the jurisdiction of EMA. Most of the core recommendations therein are seen as "must do" activities for a globally leading regulatory agency and European regulatory network with responsibility for over 500 million people across 31 countries (EU and EEA). This suggests the need to clarify what initiatives are undertaken as part of RSS 2025 and what comprises the EMA's standing operational plan, and what implications this has for resources and timing.

Key priorities and why

Important:

- Continue to support development of new antibacterial agents and their alternatives (Rec. 4.2); Industry continue to advocate for collective action to address AMR and we welcomes proposals to support the development of new medicines to combat AMR. Industry also welcome proposals to work with HTA bodies to define and explain the relevance of evidence requirements for new antibacterial medicines. The unique development challenges of antibiotics are poorly understood by many stakeholders, and industry would welcome partnership with EMA to better explain the evidentiary standards and basis for assessment.

- Promote global cooperation to anticipate and address supply problems (Rec. 4.3); The unavailability of medicinal products in the EU is frequently in the political debate at present, made more salient by the BREXIT requirements. Novo Nordisk agrees with the explanation in the RSS 2025 that the reasons for unavailability are complex and based within a global supply chain framework. The complexity reflects the fact that only some reasons have a regulatory dimension, and so it is not entirely within the remit of EMA to address these. However, there are opportunities to act. Where reasons are more related to procurement terms, it is therefore important to continue to engage with health authorities on the causes of supply shortages, as indicated in this recommendation.

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**:

Novo Nordisk considers RSS 2025 Strategic Goal 5 as an essential enabler for numerous recommendations under the previous goals. Consequently, although the goal and the recommendations as described in the consultation document seem to focus narrowly on the engagement between regulatory authorities and academics, industry also recognise the value of this goal. Moreover,we members would recommend that to truly achieve the goal of enabling and leveraging research and innovation in regulatory science, both academic and industry-based researchers should be acknowledged in this strategy. To include industry as a partner in these efforts will ensure a richer elaboration to outline and collaboration to advance the research horizon. We encourage EMA's involvement in public-private partnerships such as IMI.

Key priorities and why

Important:

• Novo Nordisk prioritises the recommendation to develop network-led partnerships with academia (Rec. 5.1) - and introduces the addition of pharmaceutical industry researchers - to undertake fundamental research in strategic areas of regulatory science. This measure can support platforms for scientific discourse and engagement including through IMI and beyond. This proposal could also be extended to include collaboration with students, as it is critical for Europe to have a pipeline of talent to support the long-term future of regulatory science.

Anything missing

The role of industry (e.g., pharmaceutical and information technology companies) in this community of research and practice should be noted, to ensure that "regulatory science remains at the cutting edge so that EMA can deliver its fundamental mission of protecting human and animal health and facilitating the availability of medicines to patients" (p. 32, RSS 2025). Any strategy to advance regulatory science related to medicines should include the principal contributors, including medicine developers. Importantly, EFPIA members including Novo Nordisk stand willing to collaborate on the European agenda to advance regulatory science, and we would welcome the opportunity to join this community of research and practice.

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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