

Public consultation on EMA Regulatory Science Strategy to 2025

EFPIA FINAL RESPONSE – submitted via email to EMA

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Word version for editing

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

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

*** Please indicate the capacity in which you are responding:**

between 1 and 3 choices

	Citizen
	Patient
	Carer
	Animal owner
	Farmer
	Individual
	Company
X	Trade association
	SME

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

Name of organisation (if applicable):

European Federation of Pharmaceutical Industries and Associations (EFPIA)

Question 2: Which part of the proposed strategy document are you commenting upon:

X	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.

Executive Summary:

EFPIA’s Emphasis on Regulatory Science:

EFPIA welcomes the opportunity to offer comment on the Agency’s *Regulatory Science Strategy to 2025* (hereafter referred to as RSS 2025). Within these comments, EFPIA identifies priorities that the innovative biopharmaceutical industry believes 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. EFPIA represents 40 research-intensive biopharmaceutical companies committed to researching, developing and bringing new medicines to patients to improve patients’ health and quality of life. EFPIA also includes direct membership of 36 national associations.

In total, there are over 7000 medicines in development (1). In Europe, these 40 companies invest 35 billion Euros in R&D (2), which comprises over three-quarters of all health industries R&D (44.8 billion Euros) (3). Once effectively implemented, EMA’s RSS 2025, will be a key enabler for bringing this promising next wave of medical innovation to patients who continue to face the burden of unmet medical need.

Critical Timing for Advancement of EMA’s Regulatory Science Strategy:

This new 5-year strategy comes at a critical juncture for the EU regulatory system and its collaborators. These next years will be defined by a new political environment with newly elected officials, following the expected BREXIT, and a new Commission mandate. This period will also be characterised by a changing landscape for regulatory science - shaped by the arrival of new technologies and new sources of evidence – which must be confronted by expanding capabilities of the global regulatory community. The imperative of new technologies (e.g., advanced therapy medicinal products (ATMPs), digital therapeutics) and new modalities for drug discovery and development (e.g., Artificial Intelligence (AI), advanced analytics, *in silico* studies) will only increase over the next five years. The next years will enable further advancement of patient-centred access to medicines in partnership with healthcare systems. Effectively treating and preventing disease and their complications will require medicine stakeholders to optimise the use of novel evidence in decision-making, leading to stronger collaboration with the patient advocacy community, health care professionals, HTA bodies and academia.

EU Regulatory System will need to Balance Process Improvements with Strategic Vision:

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. Important work is already underway to ensure that EMA delivers on regulatory performance and progress to meet the current regulatory science frontier. EFPIA encourages the EU regulatory system to continue its focus on facilitating the navigation across Committees who assess a candidate medicine at different stages of development. Essential actions have also been undertaken to advance the analytical methodological approaches to assessment, and this momentum needs to be sustained.

EFPIA's Input to Prioritise and Deliver the Regulatory Science Strategy to 2025:

Over the previous few years, EFPIA has established a proactive strategy to encourage advances to the regulatory environment essential for innovation, which focusses in the following key themes: ensure competitive world class system; evolve framework for innovation; elevate patient engagement; and expand global convergence. This strategy forms the foundation for industry's input offered here for EMA's RSS 2025. EFPIA also provides EMA with views and recommendations for the actualization of the RSS 2025. EFPIA would like to stress that these highlighted priorities are equally applicable to the **direction, urgency and future skills required by the EU national competent authorities and HMA** through the Multi-Annual Work Plan. 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**. In practice, pursuing one recommendation may imply the need to progress others. EFPIA highlights its views on the interdependencies of the various recommendations within these comments. 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.

EFPIA has followed EMA's request to highlight the goals "where the impact would be greatest" (Reference: EMA Regulatory Science to 2025: Strategic reflection [draft] released December 2018). EFPIA has concentrated on prioritising the objectives that the innovative pharmaceutical industry believe will best enable the delivery of novel medicines to patients – through the most effective, efficient, technologically advanced, informed means possible. While EFPIA acknowledges all of EMA's proposals, EFPIA's identified top priorities align with its mission to bring a continuously improved wave of innovative medicines to patients. EFPIA's identified top priorities align with its mission to bring a continuously improved wave of innovative medicines to patients. EFPIA's overall top three priorities from amongst EMA's "core recommendations" are found in the first three of the five strategic goals: *Strategic Goal 1 Catalysing the integration of science and technology in medicines development; Strategic Goal 2 Driving collaborative evidence generation – improving the scientific quality of evaluations; and Strategic Goal 3 Advancing patient-centred access to medicines in partnership with healthcare systems*).

EFPIA's Top Three Priorities for RSS 2025 (Note: EFPIA attributed the "very important" weighting only to these three top priorities. See Q7 priority weighting):

- **Recommendation: Foster innovation in clinical trials** (Rec 2.2)

Clinical trials are the foundation of drug development. Prioritising this topic will support the advancement of novel clinical trial concepts (e.g., umbrella, basket, master protocol trials, trials in small populations) and quantitative approaches (e.g. Model Informed Drug Discovery and Development – MID3), which are instrumental in bringing leading-edge medicines to patients earlier. The actions described in this recommendation provide an opportunity to remedy some of the current inflexibilities in the provision of

scientific advice and in the regulatory approval system for clinical trials. Importantly, this overarching objective also encompasses several additional priorities, which relate to new clinical evidence sources (e.g., registries, real-world data (RWD), Big Data, historical controls), measures (e.g., endpoints, biomarkers, wearable digital devices), and methodologies (e.g., MID3). EFPIA considers that this recommendation (along with associated recommendations and proposed next actions) are likewise applicable for EU NCAs in terms of their strategic involvement and future skill development.

- **Recommendation: Diversify and integrate the provision of regulatory advice along the development continuum (Rec. 1.7)**

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. This envisaged dynamic advice is also needed to adaptably accommodate specialised input for specific types of products (e.g. paediatrics, drug-device combination products). The existing scientific advice process should be improved by promoting a more interactive approach during the procedure and allowing greater access to specialised working groups when novel approaches are proposed.

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) and beyond (e.g., US FDA). The overall value of pan-EU scientific advice is undermined when contradictory opinions emerge during the development of a product. This can be through the different EMA Committees, but also, through 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 provides comprehensive guidance to companies. Consequently, today, companies must attempt to weave together advice given at multiple points along the drug development path. The entire regulatory advice process could gain from greater flexibility, iterative pathways for seeking advice, and integration in a more holistic manner. Early appointment of a Rapporteur, as in PRIME, may be an ideal method to help facilitate flexible, but integrated regulatory advice. Flexible, iterative, and then integrated advice should also benefit from engagement of and coordination with an extended group of stakeholders such as HTA and Notified Bodies.

- **Recommendation: Promote use of high-quality real-world data (RWD) in decision making (Rec. 3.4)**

In 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 and big data) for gathering RWD, methodologies necessary to ensure quality and usefulness of the data, novel analytical or quantitative techniques (e.g., AI, modelling), and ultimately the implementation of global standards. Since collaboration and alignment in this field is critical, progress and efforts should be transparent across time for all stakeholders. Acceptability builds from experience, best practice sharing and familiarity, which suggests a key role for gaining experience through multi-stakeholder collaborations such as demonstration projects (e.g., through public-private partnership platforms). Demonstration projects are essential to increase knowledge, capacity and confidence levels amongst RWD stakeholders including pharmaceutical companies and regulators. Piloted approaches are also ongoing in other countries and regions (3), and EMA should remain active in this field of research internationally. Moreover, **enhanced acceptability of RWD to support regulatory decisions** must also involve and evolve with patients, HTA bodies, healthcare professionals and other stakeholders. The EMA RSS 2025 also includes an objective to "develop a capacity that will enable the Agency to rapidly and securely access and analyse large amounts of healthcare data". It is recommended that such a capacity (e.g., system or algorithm) should be developed in consultation with relevant stakeholders including industry.

Additionally Important Recommendations:

EFPIA's top three priorities listed above address the most urgent recommendations to bring innovative new treatments to European patients. Along with these priorities, EFPIA 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.

EFPIA also highlights the recommendations to **Facilitate the implementation of novel development and manufacturing technologies** (Rec. 1.4) and **Optimising Capabilities in Modelling, Simulation and Extrapolation** (Rec. 2.6). Manufacturing of medicines is evolving to embrace new models such as continuous manufacturing and stakeholders should further collaborate to advance these approaches. Currently, at times, EU regulators seem hesitant at times 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.

Moreover, EFPIA 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.

EFPIA's Proposals to Action and Deliver RSS 2025:

Within these comments, EFPIA offers a number of prioritised, consequential actions that industry considers will ensure that implementation of RSS 2025 achieves its vision.

In order to **foster innovation in clinical trials** (Rec. 2.2), EFPIA proposes that EMA undertakes 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
- Coordinate cooperation opportunities (e.g., multi-stakeholder workshops, demonstration projects) and pilot schemes to discuss case studies with developers reflecting range of complex study designs);
- Develop further the CT Information System to best accommodate complex CTs;
- Facilitate better alignment between EU regulators in the clinical trial pathway; and
- Advance global coordination on the topic.

To **diversify and integrate the provision of regulatory advice along the development continuum** (Rec. 1.7), EFPIA suggests that EMA:

- Lead the redesign of a more flexible and integrated R&D product support mechanism;
- Enhance the coordination of advice across Committees, National Competent Authorities and other pertinent stakeholders;
- Provide preliminary feedback to the sponsor ahead of discussion meetings;
- Ensure wider stakeholder involvement;

- Consider special perspectives (e.g., paediatrics, drug-device combination products) within the advice continuum;
- Optimise usage of CT Information System (CTIS); and
- Advance acceptance of digital endpoints.

In order to **promote the use of high-quality RWD in decision making** (Rec. 3.4), EFPIA proposes actions for EMA such as:

- Launch a strategic initiative to integrate RWE in drug development, including the use of demonstrator projects to engender familiarity;
- Build on ongoing efforts (in EU and internationally) to provide clarity on scope and quality of sources of RWE;
- Seek to align and contribute to extend the standards and methodologies for collecting, analysing and validating RWE use internationally; and
- Coordinate workshops to progress RWD/E dialogue and publish workshop conclusions.

EFPIA considers that these actions will have substantially beneficial effects towards progressing RSS 2025. EFPIA continues to value and rely upon EMA’s delivery of 5-year strategic and work plans. The process to deliver RSS 2025 has been the most comprehensive regulatory science strategy development to date including the public workshop and extended consultation period. This has allowed the industry to undertake a robust approach to offer these priorities and comments. As such, EFPIA 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.

(1) EFPIA Annual Report 2018; <https://efpia.eu/media/412957/efpia-2018-annual-report.pdf>

(2) The Pharmaceutical Industry in Figures 2019: Key Data. <https://efpia.eu/media/412931/the-pharmaceutical-industry-in-figures-2019.pdf>

(3) Scoreboard 2018; <http://iri.jrc.ec.europa.eu/scoreboard18.html>. Table 3.2 p. 45. “Health industries” includes biotechnology, health care providers, medical equipment and pharmaceuticals companies (ICB4)

(4) <https://www.fda.gov/media/120060/download>

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

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

X	Yes
	No

Comments on strategic goal 1 (h):

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

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

X	Yes
	No

Comments on strategic goal 2 (h):

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

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

X	Yes
	No

Comments on strategic goal 3 (h):

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

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

X	Yes
	No

Comments on strategic goal 4 (h):

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

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

X	Yes
	No

Comments on strategic goal 5 (h):

Please note you will be asked to comment on the core recommendations and underlying actions in the subsequent questions.

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 (Rec 2.2)

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.

Rationale for Prioritisation:

EFPIA's highest prioritised RSS 2025 recommendation is **Foster innovation in clinical trials** (Rec 2.2) as industry believe it has the potential to deliver the most significant impact in the regulatory system over the next five years. In fact, this topic has been prominently included in EFPIA's regulatory priority areas for the last few 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., umbrella, basket, adaptive seamless design, master protocol or pragmatic trials, trials in small populations) 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., 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:

- **Develop the regulatory framework for emerging clinical data generation** (Rec 3.3)
- **Support developments in precision medicine, biomarkers and 'omics** (Rec 1.1)
- **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, EFPIA 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. Workshops are also needed to ensure that emerging challenges in conducting CCTs can be addressed in a timely way (e.g., any issues resulting in restrictions in making multiple substantial modifications to clinical trials, which are often necessary for CCTs). RSS 2025 also notes the objective of modernising the GCP regulatory oversight, which is a topic that should be incorporated into these workshops. For completeness, these workshops should have followed-up actions including publications of discussion outcomes (e.g., workshop white paper). 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. These types of fora should help resolve alignment issues across National Competent Authorities, ethics committees, HTA bodies and patients' organisations when considering acceptance of CCTs. Experience should also be gained through multi-stakeholder collaborations such as demonstration projects (e.g. through public-private partnership platforms).

- **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 is currently progressing the CCT concept of 'Adaptive Designs', and additional elements of CCTs could be opportune for advancement under the ICH infrastructure.

Second choice (h)

7. Diversify and integrate the provision of regulatory advice along the development continuum (Rec. 1.7)

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.

Rationale for Prioritisation:

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. 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 need for a flexible approach across the lifecycle is well demonstrated in the case of a product approved via an accelerated pathway which may require modification of a post-approval change management protocol (PACMP) to accommodate CMC changes. The potential for advice to be provided by parties familiar with the product and aware of the original risk/benefit considerations within a flexible framework is of particular importance.

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. The entire regulatory advice process could gain from greater flexibility, iterative nature of advice, and integration in a more holistic manner. Early appointment of a Rapporteur, involvement of other scientific Committees members (PDCO, CAT, COMP) and an assigned EMA contact point as in PRIME may be an ideal method to help facilitate flexible, but integrated regulatory advice. Flexible, iterative, and then integrated advice should also benefit from engagement of and coordination with an extended group of stakeholders such as HTA and Notified Bodies.

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)

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. The company may wish to receive input on only a few key questions related to a clinical study plan and currently must wait almost half a year for this advice. EFPIA 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., paediatrics, drug-device combination products)
- **Optimise usage of CT information System**. Consider how the data to be included in the CT Information System – currently being developed as part of the CT Regulation - 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.
- **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)

Third choice (h)

18. Promote use of high-quality real world data (RWD) in decision-making (Rec. 3.4)

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.

Rationale for Prioritisation:

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 (5). The recommendations from the Big Data Taskforce actually connect, not only to this Recommendation 3.4, but also, to recommendations 3.5 and 3.3 considering more widely the need to build the skills to support the use of high-quality RWD, which fits the Taskforce's definition of "big data" (i.e., 'extremely large datasets which may be complex, multi-dimensional, unstructured and heterogeneous, which are accumulating rapidly and which may be analysed computationally to reveal patterns, trends, and associations. In general, big data sets require advanced or specialised methods to provide an answer within reliable constraints').

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. Sometimes industry is asked why RWD is not more generally used in development programmes; the answer is that the current use reflects the anticipated acceptance of these evidentiary sources, generating a "chicken and egg" dilemma. 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 (6, 7, 8), and EMA should remain active in this field of research internationally. Moreover, 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' understanding of novel RWD source types, RWD quality considerations, and evolving analytical methodologies for generating RWE (especially methods applied to observational data).
 - Steps to ensure consistency in how RWD and RWE approaches are evaluated by EMA and national competent authorities. For example, FDA has established a "RWE Subcommittee" to bring about greater consistency across the agency's different review divisions.
 - EFPIA believes that advances are possible and is encouraged by the IMI GetReal Initiative, particularly the newly created GetReal Think Tank, which includes European regulatory officials and other collaborators. A formal initiative like this would signal the EMA's intent to actively progress and resource integration of RWE in regulatory decision-making.
- **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. For consideration, recent examples for RWE have been held in the US, leading up to the FDA's guideline development (9).
5. Published February 13, 2019. https://www.ema.europa.eu/en/documents/minutes/hma/ema-joint-task-force-big-data-summary-report_en.pdf
 6. <https://www.fda.gov/media/120060/download>
 7. <https://www.rctduplicate.org/>
 8. <https://www.focr.org/rwe/>
 9. The US National Academies of Sciences, Engineering and Medicine (NASEM) and Duke Margolis series of workshops

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

Although the **relevance to post-authorisation regulatory and safety science** is implicit in many of the recommendations, it would be valuable to make these links **more explicit** in the texts as well as the

underlying planned actions. To do so will underscore the lifecycle approach to innovation that the Agency is taking for regulatory science.

For example, the recommendation **Expand benefit-risk assessment and communication** (Rec. 2.4) identifies the need for systematic application of structured benefit-risk methodology and quality assurance systems across the network, including improved communication with HTA bodies. However, this could be elaborated also to consider post-authorisation assessment, considering new evidentiary sources and the need to improve the analytics and evaluation of these data to better identify and isolate meaningful safety signals for action.

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)

Recommendation	Very important	Important	Moderately important	Less important	Not important
1. Support developments in precision medicine, biomarkers and 'omics'		X			
2. Support translation of Advanced Therapy Medicinal Products cell, genes and tissue-based products into patient treatments			X		
3. Promote and invest in the Priority Medicines scheme (PRIME)		X			
4. Facilitate the implementation of novel manufacturing technologies		X			
5. Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products		X			
6. Develop understanding of and regulatory response to nanotechnology and new materials' utilisation in pharmaceuticals			X		
7. Diversify and integrate the provision of regulatory advice along the development continuum	X				

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:

Key priorities and why

Scientific advances and new technologies (e.g. system biology, in silico trials and functional imaging) 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.

EFPIA shares the vision that sees the Agency at the crossroads between science and healthcare (10) 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 intent of this strategic goal can be achieved only by adapting the regulatory advice platforms currently available. RSS 2025 Strategic Goal 1 is central to deliver the promise of new prevention and treatments for life-limiting disease. The recommendations under RSS 2025 Strategic Goal 1 capture key areas through which effective regulation can translate excellent science into available care. EFPIA offers comment on several of Goal 1's recommendations: EFPIA 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 EFPIA's Top Priorities see answer to Question 5 – second choice

Important:

- **Support developments in precision medicine, biomarkers and 'omics (Rec. 1.1);** EFPIA welcomes the core recommendation to **Support developments in precision medicine, biomarkers and 'omics'** and in particular the underlying action to 'Evaluate...biomarker impact on clinical outcomes'. 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. Dedicated expert group discussions, routed in the reality of clinical practice, would help EMA and downstream regulators to align their views.

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

Certainly, EFPIA considers the PRIME scheme as an especially promising approach to bringing new products to patients for unmet medical need as early as possible. EFPIA 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. PRIME offers early scientific input and ongoing dialogue. Recent trend data demonstrate that EMA's product review timelines are getting longer, and indeed, are notably longer compared with US (11).

The first marketing authorizations for products designated as eligible to PRIME were granted only in June 2018; hence 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. EFPIA concurs that involvement of HTA bodies in PRIME is key to ensure that scientific advice takes into account the generation of data along the development lifecycle to satisfy the needs of downstream decision makers on reimbursement and access. In terms of capacity building to ensure that all applicants would continue to see the benefit of using the scheme, it is suggested that a "fast lane" approach would be designed for PRIME products which would include: shorter timeline for eligibility and kick-off meeting, continuous access to EMA contact person, dynamic opportunities to receive advice on product development. EMA should fully consider the learnings and recommendations from the 2018 EMA/FDA PRIME workshop in London.

- **Facilitate the implementation of novel manufacturing technologies (Rec. 1.4);** As highlighted in earlier in EFPIA's comments, manufacturing of medicines is evolving to embrace new models such as continuous manufacturing. 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. 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.
- **Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products (Rec. 1.5);** EFPIA strongly supports the proposal to create an integrated evaluation pathway for medicine-medical device combination products and 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.

Moderately Important:

Relatively lower priority is given to the recommendation on nanotechnology and new materials in pharmaceuticals primarily because these areas are already reflected in ongoing initiatives by EU regulators. Also, relatively lower priority is given to the recommendation on ATMPs as this reflects a development focus for only a subset of EFPIA members. EFPIA recognises that EMA already has extensive ongoing activities in support of ATMPs which industry expects will continue.

Anything missing

Nothing noted.

Proposed specific actions

Please note EFPIA's proposed actions for **Diversify and integrate the provision of regulatory advice along the development continuum** under question 5 above. These proposals transect a number of recommendations under RSS 2025 Strategic Goal 1.

(10) From Professor Guido Rasi's presentation at ICMRA:

<https://www.pmda.go.jp/files/000220949.pdf>

(11) Centre for Innovation in Regulatory Science; R&D Briefing 70; New drug approvals in six major authorities 2009-2018: published 29 May 2019; http://www.cirsci.org/wp-content/uploads/2019/05/CIRS-RD-Briefing-13052019_for-send-out.pdf [accessed 30 May 2019]

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

Recommendation	Very important	Important	Moderately important	Less important	Not important
8. Leverage novel non-clinical models and 3Rs			X		
9. Foster innovation in clinical trials	X				
10. Develop the regulatory framework for emerging digital clinical data generation		X			
11. Expand benefit- risk assessment and communication			X		
12. Invest in special populations initiatives			X		
13. Optimise capabilities in modelling and simulation and extrapolation		X			
14. Exploit digital technology and artificial intelligence in decision-making		X			

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:

Key priorities and why

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.

EFPIA 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, EFPIA'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)**- EFPIA's 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.

- **Exploit digital technology and artificial intelligence in decision making (Rec. 2.7);** Healthcare is currently implementing novel technologies such as digital technologies and artificial intelligence (AI), which have been used in other sectors for a number of years. By 2025, AI and machine learning will have been used in many areas of medicine development and regulation. This area needs focus and resourcing.

Moderately Important:

While still considered of importance since evidence generation is a continuum, the following recommendations are of lesser priority to EFPIA.:

- **Leverage non-clinical models and 3Rs principles (Rec. 2.1);** there is work ongoing to identify better approaches in the EU and internationally. Nevertheless, EMA is encouraged to continue collaborating, and EFPIA is pleased to offer support as appropriate.
- **Expand benefit-risk assessment and communication (Rec. 2.4);** EFPIA welcome this recommendation to incorporate patient preferences and improve communication with HTAs bodies. There are a number of initiatives ongoing at the Agency on this topic, including participation in related IMI projects. EMA is encouraged to continue current initiatives and consider how benefit-risk assessment and communication will need to evolve to incorporate the above priorities with the support of all concerned stakeholders. In particular EMA is encouraged to advance Science and Methodology alignment on gathering the patient preferences / the relevance of Benefits and Risks from patient perspective.
- **Invest in special populations initiatives (Rec. 2.5);** EMA is encouraged to continue 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 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.

Anything missing

- Nothing of note

Proposed specific actions

- Please note EFPIA's proposed specific actions for fostering innovation in clinical trials under question 5 above. These proposals transect a number of recommendations under RSS 2025 Strategic Goal 2.

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

Recommendation	Very important	Important	Moderately important	Less important	Not important
15. Contribute to HTAs' preparedness and downstream decision-making for innovative medicines		X			
16. Bridge from evaluation to access through collaboration with Payers				X	
17. Reinforce patient relevance in evidence generation		X			
18. Promote use of high-quality real world data (RWD) in decision-making	X				
19. Develop network competence and specialist collaborations to engage with big data		X			
20. Deliver real-time electronic Product Information (ePI)		X			
21. Promote the availability and uptake of biosimilars in healthcare systems				X	
22. Further develop external communications to promote trust and confidence in the EU regulatory system			X		

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 EFPIA members strongly support. EFPIA recognises 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.

At its core, this strategic goal is seeking to better utilize evidence in healthcare systems to support effective regulatory procedures and decision-making, from the patient's view. As such, EFPIA considers

that some of the recommendations initially identified under goal 3 to be of higher potential benefit compared with others.

Key priorities and why

Very Important:

- **Promote use of high-quality real-world data (RWD) in decision making (Rec. 3.4);** EFPIA'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, EFPIA 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);** EFPIA 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) (3.6);** There is important work already underway to progress the ePI and EFPIA is engaged and supports these efforts though the Inter-Association Task Force formed by the industry, in partnership with EMA and HMA.

Moderately Important:

As set out in the guidance for the review of the RSS 2025, collaborators are given the task to prioritise amongst the recommendations across the 5 Strategic Goals. EFPIA also recognises that EMA cannot embrace all of the initiatives in draft simultaneously. Accordingly, EFPIA have afforded less priority to initiatives which are already underway at the Agency and/or would be expected to continue as "business as usual":

- **Further develop external engagement and communications to promote trust and confidence in the EU regulatory system (Rec. 3.8);** Again, although EFPIA fully recognises that this initiative is essential as a means to deliver the RSS 2025, this is continuing work already undertaken by EMA. For example, the recent inquiry by the European Ombudsman on pre-submission activities highlights the importance of this engagement and communication in order to deliver on the goals of the RSS.

Less Important:

EFPIA have given less priority to initiatives which are better addressed to procurement decision-making, which should be undertaken by other agencies at the EC and national level:

- **Bridge from evaluation to access through collaboration with payers (Rec. 3.2);** Whilst the engagement is important, EFPIA has given lower priority to the recommendation for EMA to bridge

from evaluation to access through collaboration with payers. Regulatory processes and regulatory determinations should maintain their distinctiveness from decision making for different purposes (pricing, terms of access). EFPIA does not want the scientific focus of regulators to be detracted. The opportunity for determining the value of a medicine in healthcare follows that important regulatory decision, and this opportunity is appropriately based in the specific context in which healthcare is delivered.

Payers are a fundamental decision-maker with regard to access to medicines, and there are benefits to engaging with payers earlier, to gain insight into their perspectives on unmet needs and priorities. Early engagement may help to prepare payers for potential impacts from breakthrough innovation. Of course, it is at the discretion of each individual company – rather than regulatory officials - to engage with payers in light of their portfolio and planning to pursue this engagement at the most suitable time.

- **Promote the availability and support uptake of biosimilars in healthcare systems (Rec. 3.7);** EFPIA recognises the leading role in which EU regulators have played to pioneer the “biosimilar concept”; the principles of which have been replicated and adopted by regulators around the world. However, EFPIA does not consider that promotion of the availability and uptake of biosimilars in healthcare systems to be a regulatory science topic. EFPIA supports EMA’s efforts to promote the solid framework for biosimilars approval in EU, which is based on scientifically-appropriate approval standards and robust pharmacovigilance measures that put patient safety first.

Anything missing

Nothing noted.

Proposed specific actions

Please note EFPIA’s proposed actions for promoting the use of high-quality real-world data (RWD) in decision-making under question 5 above. These proposals transect several recommendations under RSS 2025 Strategic Goal 3.

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

Recommendation	Very important	Important	Moderately important	Less important	Not important
23. Implement EMA's health threats plan, ring-fence resources and refine preparedness approaches			X		
24. Continue to support development of new antimicrobials and their alternatives		X			
25. Promote global cooperation to anticipate and address supply challenges		X			
26. Support innovative approaches to the development and post-authorisation monitoring of vaccines		X			
27. Support the development and implementation of a repurposing framework				X	

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 EFPIA strongly supports (e.g., AMR, vaccines and supply challenges). As such, EFPIA has 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 by EFPIA members 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. EFPIA 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. EFPIA also notes the link to the importance for development of better diagnostics to improve stewardship and limit diseases.

- **Support innovative approaches to the development, approval and post-authorisation of vaccines (Rec. 4.4);** EMA has a critical role to play in enabling new vaccines to become developed and accessible to the populations in need and the vaccine industry. EFPIA sees opportunities for the advancement of methods/tools (e.g. biomarkers) to characterise immune response, which should: 1) facilitate the identification of correlates of protection and surrogate markers which will enable the development of innovative vaccines, and 2) support the development of new approaches such as *in vitro* methods to identify measurable characteristics of product safety, quality, and potency. Promoting innovative clinical trial design will allow vaccine developers to demonstrate positive benefit/risk with a reduced number of subjects recruited in phase III trials is key to deliver new vaccines quicker to the patients. For HTA bodies, it is equally important to pursue systematic early and continuous open dialogue with EMA, public health authorities and NITAGs to better inform decision-making. Another initiative under this recommendation addresses the difficulty to generate post-approval effectiveness data in Europe; establishing a platform for EU benefit-risk monitoring of vaccines post-approval will deliver benefits for all stakeholders, and a review of the IMI's ADVANCE and DRIVE programmes can support that effort. Finally, again linked with Recommendation 3.8 (promote trust and confidence), the goal to communicate proactively with key stakeholders on benefit-risk using evidence-based tools to tackle vaccine hesitancy is an essential measure for public health.
- **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. EFPIA agrees strongly 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. The unavailability of medicinal products in the EU is frequently in the political debate at present, made more salient by the BREXIT requirements. EFPIA agrees strongly 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. EFPIA welcomes the setting up of a pilot phase when the HMA/EMA guidance on shortage notification will become effective. This pilot phase is essential for industry to adapt internal processes to ensure compliance with the guidance and for both industry and regulators to test the concepts and requirements described in the guidance in view of proposing improvements if necessary. 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. EFPIA members would also link this recommendation to two others: Recommendation 1.4 (novel manufacturing technologies) and (Recommendation 3.6 (electronic product information ePI), both of which could offer flexibilities in the supply chain to better address the causes for unavailability of medicines.

Anything missing

Nothing noted.

Proposed specific actions

In addition to those identified under the recommendations prioritised:

- To support AMR, EFPIA supports opportunities for joint scientific advice with HTA bodies and the publication of articles to explain evidentiary standards and the basis of assessment

for antibiotics and how they differ from other therapeutics.

- To support supply flexibility in medicines and vaccines, consider ePI pilot to assist with supply availability across Member States

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

Recommendation	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		X			
29. Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions			X		
30. Identify and enable access to the best expertise across Europe and internationally			X		
31. Disseminate and share knowledge, expertise and innovation across the regulatory network and to its stakeholders			X		

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:

EFPIA 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, EFPIA 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.

Key priorities and why

Important:

- EFPIA 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.

Moderately Important:

- Although EFPIA has given less priority to the other recommendations, this simply reflects that industry believe that the first Recommendation 5.1 is the pivot upon which all the subsequent actions will rest. EFPIA notes that Recommendation 5.2 (**Leverage collaborations between academia and network scientists**) also includes some welcome focus on ring-fencing investment for emergent scientific challenges; however, focusing on the link only between network scientists and academia to provide translation from applied research into new drug products and regulatory tools seems too narrow a focus. Industrial researchers could play a material role in supporting EMA and academia to stay at the cutting edge of these emerging innovations.
- **Identify and enable access to the best expertise across Europe and internationally** (Rec. 5.3): EFPIA considers this recommendation key to review complex and innovative dossiers.
- **Disseminate and share knowledge, expertise and innovation across the regulatory network and its stakeholders** (Rec. 5.4): As a key contributor to scientific advances, industry would appreciate involvement in opportunities the exchanging of knowledge and sharing of expertise.

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 stand willing to collaborate on the European agenda to advance regulatory science, and industry would welcome the opportunity to join this community of research and practice.

Proposed specific actions

- Include pharmaceutical industry researchers in the network-led partnerships that direct priority areas for fundamental research based on the regulatory science strategy (e.g., PROs, ‘omics, AI, drug-device combinations, M&S).

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