EPF response

EMA – Regulatory Science to 2025

1. **Do you consider the EMA's Strategic Goals appropriate?**

Comments:

EPF considers that all above goals are relevant. However, we believe that further improving the system for medicines safety monitoring and reporting of side effects – pharmacovigilance – should be included explicitly as a key goal and action area, as it is crucial for patient safety and public health.

Furthermore, we would like to point out the lack of mention of meaningful, structured and systematic involvement of patients in each of the strategic goals. This in itself does not invalidate the goals but is a missing element that needs to be incorporated. We make proposals for each goal separately, below.

2. **What are the 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?**

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

"Reinforce patient relevance in evidence-generation". Currently, patients' priorities are too little taken into account in clinical trials design, resulting in clinical trials data that may not include patient-relevant endpoints. Quality of life is often not adequately reported. Embedding patient priorities into clinical trials design, via clear EMA guidance co-developed with patients, is needed to ensure that meaningful data is generated for regulatory assessment. It is also important for bridging the evidence gap between marketing authorisation, HTA and payers. Linked actions are needed to enhance benefit-risk assessment with more integration of patient perspectives and patients' input; develop a regulatory framework for digital clinical data generation; and promote the use of high-quality real world data which should include patient-generated data. There is also a link and synergy with improved patient input into developing information and communication on medicines.

Please comment on your 2nd choice, the underlying actions proposed, and identify any additional actions you think might be needed to effect these changes:

"Contribute to HTAs' preparedness and downstream decision-making for innovative medicines." There is currently an evidence/data gap between regulatory requirements and those of HTA bodies, which impedes swift evaluation of new medicines and patients' access. We see a need to integrate discussions about the evidence and data requirements of all of these decision-points much earlier into the clinical development of a medicine. This would also require actions to enhance collaboration with payers and improve the provision of regulatory advice along the development continuum, with the involvement of HTA, payers, patients and healthcare professionals.

Please comment on your 3rd choice, the underlying actions proposed, and identify any additional actions you think might be needed to effect these changes:

"Deliver real-time electronic Product Information (ePI)." Patients need and want more up-to-date, accessible, tailored and interactive information on medicines. Delivering real-time electronic product information is important but should not only be limited to putting package leaflets online; rather it should also include a more in-depth review of the PIL to ensure it is really "fit for purpose" for informed decision-making, in line with the recommendations of the European Commission's 2017 report and the PILS and PILS-BOX studies commissioned by the European Commission. Patients' involvement and input in developing statutory product information and labelling should be improved. Currently, patient review of package leaflets comes too late and is limited to one or two reviewers; patients' comments can often not be taken into account because of the constrained format of the PIL; and there is no systematic approach to user-testing the PIL.

Are there any significant elements missing in this strategy? Please elaborate which ones:

EPF believes pharmacovigilance is a significant missing element. One of the EMA's key tasks is to oversee the European system for medicines safety monitoring and reporting of side effects. In particular, we see the need to ensure effective communication of side effects both in clinical trials results (including the "lay" versions intended for patients and the general public), understandable and actionable information on side effects on medicines' package leaflets, and supporting greater patient involvement in pharmacovigilance and in reporting of side effects.

The strategy also misses another significant element: the meaningful, structured and systematic involvement of patients needed to realise each of the strategic goals. The Agency's Chief Executive Guido Rasi recently stated the EMA will play its role to make patient engagement the norm by 2025. EPF welcomes this important statement of intent. The EMA has been at the forefront of patient involvement in medicines regulation in the EU, but this is a fast-advancing area and EPF believes the current strategy needs to be more explicit and more ambitious in this regard. The strategy to 2025 should set standards for all actors in medicines research, development and evaluation. It should include concrete elements that will contribute to the goal of making patient engagement the norm, including specific activities, expected outcomes and an evaluation approach.

A third element of priority to patients, that is missing from the EMA strategy but is very high on the EU agenda and in patient advocacy, is data sharing, development of patient registries and specifically of disease registries instead of the current model of product registries. At the same time, promotion of the FAIR Data principles will promote research and liberate valuable patient data that are currently siloed by various stakeholders. The disease registry discussion can include the pharmacovigilance aspect promoting adverse event reporting and safety, but also head-to-head efficacy monitoring. Optimal use and reuse of the data available to EMA is also a serious concern for the patient. Utilizing these datasets for research can be very useful especially in small population trials.

Strategic goal 1 – Catalysing the integration of science and technology in medicines development

Comments:

EPF sees precision medicine, biomarkers, cell and tissue therapies as important emerging treatment classes, so this as well as the related evaluation pathway are high priorities. However, "personalised" medicine is not only about precision medicine, and it needs a comprehensive approach that avoids fragmentation. "Omics" is a promising field where the convergence of science and technology can

offer innovative solutions, provided it is organised in a structured and exploitable way across Europe. We also draw attention to the way technology can transform the relationship between patients and healthcare professionals in various ways, for example in terms of information, communication, shared decision-making and ethical issues; any regulatory strategy should take into account these impacts. Collaboration with the research community is necessary, but not sufficient to realise these objectives. As the end users of medicines, patients should occupy a central and active role in the development and evaluation of medicinal products and technologies, as well as the underlying evidence-generation, bringing their knowledge and experience to the evaluation process. The EMA as the EU's regulatory body should make patient involvement explicitly a *sine qua non*, open up opportunities for patient involvement and provide clear guidance to both industry and academic researchers. Finally the EMA should ensure that there are no conflicts of interest in the integration of science and technology in medicines development, as in other areas.

Strategic goal 2 – Driving collaborative evidence generation – improving the scientific quality of evaluations

Comments:

We consider it important to foster innovation in clinical trials, and see the role of EMA as ensuring the high quality of evidence on safety, efficacy and quality. It may be an important area to look at adaptive or pragmatic clinical trials designs in this context and see how the best possible evidence can be generated. Digital clinical data should include patient-generated data and its integration into high-quality regulatory assessment. Patients and patient organisations should be involved systematically to ensure full integration of real world data as an integral part of the "life cycle" of medicines.

Patients are a key stakeholder group that needs to be engaged in all activities and this is currently missing from the strategy. Innovation is also about finding better ways of doing things, and innovating meaningful, structured and systematic patient involvement should be a key responsibility of the EMA. Patient involvement brings added value to innovations in clinical trials, data generation and benefit-risk assessment, as well as communication.

We support actions on paediatric and geriatric medicines as well as women who are pregnant or breastfeeding, including generation of improved safety data. For better understanding of diseases across the board, the EMA should encourage investment in the development of treatment solutions addressing the needs of potentially vulnerable or under-served groups of patients, including the above. Finally, EPF believes it is important to advance on non-clinical models and on the 3R principles (to replace, reduce and refine animal testing).

Strategic goal 3 – Advancing patient-centred access to medicines in partnership with healthcare systems

Comments:

EPF agrees that patients' access to new and better medicines should be a high priority. However, a more inclusive decision-making process must involve patients as key partners. Reinforcing the patients' role in evidence generation and in all related processes should be a high priority. Patients' involvement in clinical trials should be ensured from setting the research agenda to the design and conduct of trials. Quality of life and burden of the disease for the patient must be better addressed in clinical trials, with appropriate measures and endpoints that are co-developed with patients and validated to ensure they are relevant and meaningful. The EMA should pose a clear requirement for

meaningful patient involvement in all clinical trials used for regulatory purposes, and provide clear guidance to industry, written together with patients. The EMA should furthermore play an appropriate role to encourage meaningful patient involvement in HTA and related processes at national level.

On real-world data and evidence, we would like to see the development of a framework to ensure the uptake of high-quality real-world evidence by regulators; harmonisation of patient registry requirements can be a driver in this respect. Communication for trust and confidence is a key priority. Transparency of the EMA's work and processes, and visible patient participation in all activities and governance should help improve trust in regulation. Transparency of clinical trials is also vital. Patients can play a role in ensuring effectiveness in communication. Electronic product information should be efficient and user-friendly, as well as being interoperable with other eHealth applications in the EU, including ePrescriptions and Electronic Health Records. However, regulatory information for patients on medicines needs to be further developed, going above and beyond "e-PI", to make it more fit for purpose. This should be done in close partnership with patients and patient representatives.

Strategic goal 4 – Addressing emerging health threats and availability/therapeutic challenges

Comments:

For EPF the most important objectives under this goal relate to repurposing of medicines, and collaboration on addressing medicines shortages, including supply challenges and the availability of all medicines (including old as well as new medicines) to patients. Supporting research and development of new antibiotics is also a high priority in this area. Patient involvement in this area should be further developed and described. Further support and development of the repurposing framework is a priority for the patients.

Strategic goal 5 – Enabling and leveraging research and innovation in regulatory science

Comments:

EPF believes these are important actions, but they are also highly inter-linked. Dissemination and sharing of knowledge should flow from enhancing partnerships and collaborations, and identifying the best expertise. Communicating knowledge, expertise and latest developments in medicinal products is key in helping patients make informed and safe decisions. Such initiatives can improve the coordination among regulators and stakeholders and enhance the understanding and enforcement of legislation. The strategy mentions engagement between regulators, funders and academia, but omits mention of patients. The patient perspective and patients' involvement is required to ensure that the most relevant knowledge and expertise is leveraged in regulation. Academic stakeholders are often in need of training on how to work with patients; the EMA could provide a useful platform for interaction and understanding, promoting partnerships between patients and academia and to encourage researchers to practice meaningful patient involvement. The EMA should do so with the involvement and support of patient representatives at the Agency – including the PCWP, the scientific committees and management board.