European Federation of Pharmaceutical Industries and Associations

EFPIA position on the use of artificial intelligence in the medicinal product lifecycle

October 2024

Executive summary

EFPIA believes in the potential of applying AI to deliver benefit for patients, life science companies and society. AI will have a growing role in the research, development and manufacturing of medicinal products. This means we can discover and deliver new, safer, more effective treatments to patients faster than ever before.

It is critical that the regulatory frameworks governing the use of AI in the medicine development lifecycle are tailored, fit-for-purpose, risk-based, non-duplicative and globally aligned. This would ensure that rules enable, rather than hinder, the development of safe and effective treatments that reach patients more efficiently.

To realise the potential of AI in medicine development, EFPIA is proposing six key recommendations:

1. **Existing EU regulations, guidance and frameworks for medicines to be leveraged when applying AI.**
2. **The regulatory oversight for the application of AI in medicine development to be within the remit of the European Medicines Agency (EMA).**
3. **Clarity to be provided on EMA's risk-based approach to the use of AI in the context of the regulatory framework for medicines.**
4. **AI policies that balance transparency and protection of innovation when sharing information related to AI models and datasets.**
5. **Globally aligned regulatory approaches through collaboration among health authorities to foster innovation and support development of safe and efficacious medicines.**
6. **Fostering trust and capability in AI use in medicines research and development through close collaborations among industry, regulators, patients and other stakeholders.**

Our ultimate goal for **AI governance is to have suitable and risk-based guidance for oversight that is tailored to the regulatory status and specific context of use.**

EFPIA would like to underscore the significance of engaging all relevant stakeholders at the highest level in this initiative. We strongly urge early alignment on establishing a multi-stakeholder platform to meet at least twice a year to enable cross-stakeholder sharing of experience on the applications of AI in this space to foster more rapid learning on all sides.

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Introduction

Artificial intelligence (AI) can play a critical role in medicine development. Insights from AI-enabled tools will shape several aspects of the development lifecycle and healthcare delivery.

Within the innovative pharmaceutical industry there are currently significant efforts under way to optimise medicine development using a range of methodologies and tools including those incorporating AI. The industry is using these tools to optimise complex processes, leading to more effective and efficient development pathways. The application of these innovative approaches **builds on existing methods, good research practices and requirements which currently apply** (such as traditional statistical methods and approaches, including model-informed drug development).

Various forms of computer-aided methodologies, such as machine learning (ML), robotic process automation, and natural language processing have been used in medicines development for decades. However, it is the more recent advancements in technology and computing power, as well as broader access to data, that have now given rise to a wider range of novel AI approaches – such as generative AI and analytical AI – being explored across the medicines lifecycle.

As AI technology continues to advance at a rapid pace, it has become an increasing focus for legislators and for regulators. The EU has been a forerunner in this space, passing the EU AI Act, the world's first comprehensive legislation on AI, which entered into force on August 1st, 2024. **The EMA has published an artificial intelligence work plan that includes a multitude of actions from 2023 to 2028.** The work plan is focused on four dimensions: guidance**,** policy and product support; AI tools and technology; collaboration and change management; and experimentation.

In 2023, as part of the AI work plan, the EMA published a draft reflection paper on the use of AI to support the safe and effective development, regulation and use of medicines. EFPIA welcomed the stakeholder consultation opportunity on the draft reflection paper. The final version[1] was released in September 2024 with further upcoming guidance expected on the use of AI in the medicines lifecycle.

In this position paper, EFPIA is presenting **policy recommendations in relation to the use of AI in the medicines lifecycle (defined as including research and development (R&D), manufacturing and post-approval activities)**, such as EMA regulatory oversight, applicability of existing regulatory frameworks, and global harmonization.

EFPIA aligns with the Organisation for Economic Cooperation and Development (OECD) definition of an AI system (which the EU AI Act also adopted): "a *machine-based system designed to operate with varying levels of autonomy, that may exhibit adaptiveness after deployment and that, for explicit or implicit objectives, infers, from the input it receives*, *how to* generate outputs such as *predictions, content*, *recommendations*, *or decisions that can influence physical or virtual environments"*.

[1] https://www.ema.europa.eu/en/about-us/how-we-work/big-data/artificial-intelligence#ai-in-medicinal-product-lifecycle-reflection-paper-68368

AI in the medicines lifecycle & regulator remit

EFPIA considers AI systems used in the medicines lifecycle to be any AI-enabled tool or model developed and utilized to support the research, development, manufacturing, use and/or monitoring of a medicine. The application areas therefore range from pre-authorisation (discovery, R&D, QMS, nonclinical and clinical development) to post-authorisation (such as manufacturing and pharmacovigilance).

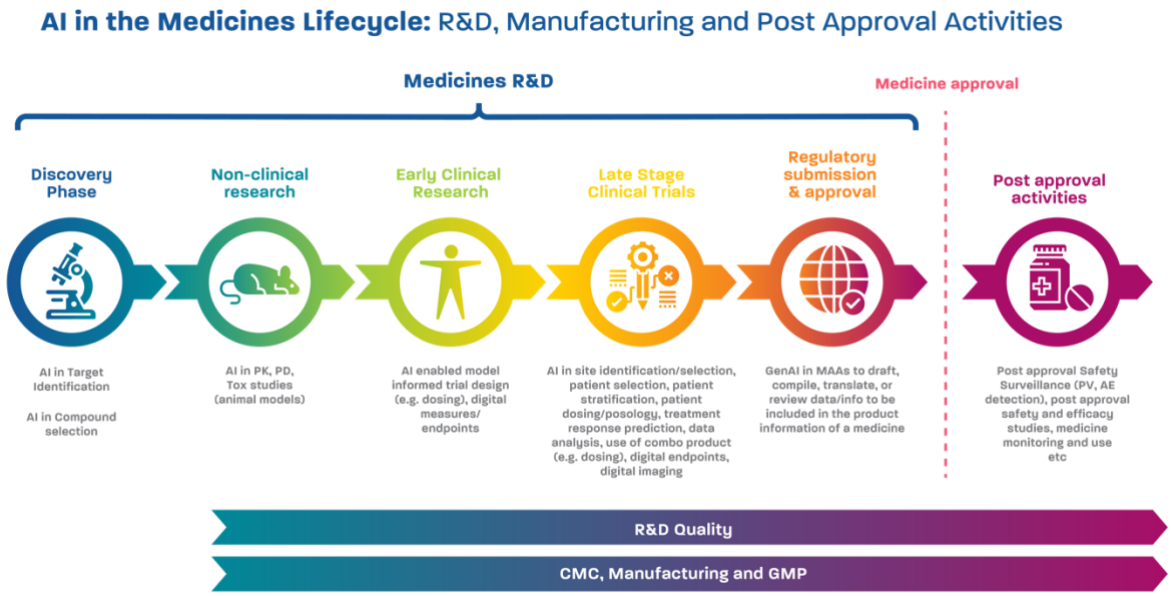

Figure 1. AI is being explored across all steps of the medicines lifecycle

This scope matches the scope of AI uses as outlined by the EMA in their reflection paper on the use of AI in the medicinal product lifecycle[2]. However, EFPIA agrees with the EMA's proposal that the trigger for their regulatory oversight of AI should be those areas that do not impact benefit-risk or regulatory decision-making. Thus, other areas – where there is no such impact – are out of the scope of the EMA and National Competent Authorities remit. For example, to quote the EMA's draft reflection paper, "*The application of AI/ML in the process of drug discovery can be low regulatory impact if non-optimal performance only affects the developer*".

The scope of this paper focuses exclusively on EFPIA's recommendations related to those areas **of AI application that may impact the benefit-risk assessment, safety or the associated regulatory decision-making.**

EFPIA believes that the ultimate goal for governance of AI should be fit-for-purpose, risk-based, non-duplicative, globally aligned regulatory frameworks for oversight which are calibrated to the regulatory status and context of use.

As we collectively enter a new era of AI policy for medicines development, with the EMA's upcoming guidance on AI in clinical development and pharmacovigilance, EFPIA is proposing the following six

[2] https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf

key policy recommendations for the EMA and the broader European Medicines Regulatory Network (EMRN) to consider.

Policy recommendations

1. Existing EU regulations, guidance and frameworks for medicines should be leveraged when applying AI

EFPIA considers that the existing, well-established EU regulatory and policy environment which governs medicine development and authorisation (consisting of well-established legislation, regulatory guidance and frameworks) can also be leveraged for the use of AI as a tool in the medicines lifecycle.

The EMA has a long-standing record of approving safe and effective medicines, many of which utilized novel and innovative technologies, tools and approaches in their development and approval. EFPIA believes the introduction of AI approaches in medicines development should be incorporated into existing development and approval processes. **EFPIA believes these existing frameworks, coupled with future EMA guidance on AI and EMA meeting interactions, will be sufficient to address any gaps in information and guidance to accommodate the inclusion of AI tools in the lifecycle of medicinal products**. Further, we support such an approach as it would lead to regulatory oversight that is based on existing regulatory standards, while being both flexible and responsive to fast-moving technology.

These existing and future regulatory frameworks and policies include, but are not limited to: the creation of regulatory sandboxes *(time-limited regulatory frameworks that allows the testing of innovative technologies)* in the context of the European Pharmaceutical Legislation revision[3]; the EMRN approach to AI as outlined in the EMA/HMA AI Workplan[4]; upcoming EMA guidance on the use of AI in the medicines lifecycle; and industry engagements with the EMA Quality Innovation Group (QIG).

In addition, applicants and developers can already discuss AI applications in the context of the lifecycle of a medicinal product with regulators via existing types of interactions including, scientific advice procedures for product specific development; the qualification pathway for novel methodologies; Innovation Task Force meetings for early interaction on innovation; or exchange with CTCG (Clinical Trials Coordination Group) ahead of a CTA (Clinical Trial Application) review and others.

2. Regulatory oversight for the application of AI in the medicines development lifecycle should be within remit of EMA

EFPIA considers that there is no legal obligation to require regulatory oversight through the AI Act for specific uses of AI systems that are solely for the purpose of medicines R&D. **EFPIA supports a sector-specific approach to regulatory oversight of AI use in the medicines development lifecycle.**

The EMA is the sole European authority with deep knowledge of the biopharmaceutical sector and R&D processes of medicinal products. The biopharmaceutical sector has a strong track record of working with the EMA and EMRN in establishing best practice guidelines and implementing

[3] https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en

[4] https://www.ema.europa.eu/en/news/artificial-intelligence-workplan-guide-use-ai-medicines-regulation

regulations. Historically, these resources contribute to the assessment and improvement of regulatory oversight of AI and drive the development of a safe and effective AI ecosystem in Europe.

The EU AI Act governs AI systems placed on the EU market or put into service. Under the AI Act, most AI-enabled medical devices which also classify as an AI system will be considered high-risk AI systems (i.e. those that need to undergo third party conformity assessment). Such devices are subject to the Medical Device Regulation (MDR)/In Vitro Medical Device Regulation (IVDR) frameworks, in addition to the AI Act.

In the context of using AI for medicines development, EFPIA considers that when used solely for the purpose of medicines R&D, AI systems are exempt from the requirements of the EU AI Act. The EU AI Act supports innovation and freedom of science and should not undermine R&D activities. This is why AI systems and models specifically developed and put into service for the sole purpose of scientific R&D are excluded from its scope (as described in Recital 25, Articles 2.6 and 2.8). The use of AI-enabled technologies for the purpose of R&D is discussed with regulators via existing types of interactions (such as scientific advice procedures) which are the best forums to address context-specific uses and assess holistically all processes applied in a highly regulated sector.

If the exemption were not to apply, EFPIA assesses that most uses of AI in medicines R&D typically involve AI-enabled software that is not regulated under any of the product-specific legal frameworks outlined in Annex I (including those for medical devices) nor are they featured under Annex III high-risk uses. Therefore, **they cannot legally qualify as high-risk under the AI Act**.

Nevertheless, whether medicines R&D is considered in scope of the AI Act under the R&D exemption or not, industry will still be applying the stringent existing regulations, guidance and policies which apply to medicines development, as appropriate, especially in GxP areas such as clinical development and pharmacovigilance, and include oversight of the use of innovative drug development tools including AI.

In summary, we believe that upcoming **AI guidance from the EMA in conjunction with the established, well-functioning legislative and regulatory frameworks for medicines will ensure an appropriate regulatory framework for AI used in the lifecycle of medicines.**

3. Clarity on EMA's risk-based approach to the use of AI in the context of the medicines regulatory framework

EFPIA supports the EMA's suggestion in the reflection paper on AI in medicines that a **risk-based approach considering risk to patient safety and potential impacts on regulatory decisions should be adopted for the oversight of AI-based drug development tools**.

However, it is essential to provide more clarity on **how the EMA defines and assesses the relative risk of AI** (in the context of application of medicines legislation) **for different uses in the lifecycle of medicines, and the framework being used for such assessments.** To clarify, EMA should provide examples of risk assessments for AI use cases across the medicines lifecycle to foster understanding among stakeholders. We believe risk should be assessed based on how the AI is applied within a specific context of use, **taking account of the influence of the AI model on patient safety, benefit-risk assessment, and/or regulatory decisions**, and possible impact on the integrity of data supporting a marketing application. The amount of evidence required to mitigate risks, and to validate and establish the credibility of the AI application, should be proportionate to the assessed risk.

We note that several risk assessment frameworks exist across the medical product lifecycle and the EMA's Committee for Medicinal Products for Human Use (CHMP) has already provided qualification advice and opinions on multiple AI/ML based tools[5], under the process for Qualification of Novel Methodologies (QoNM) for medicine development. EFPIA supports the futureproofing of the QoNM Action Plan that was published in September 2024, in line with the EMA's Network Strategy to 2025 and EMA Regulatory Science Strategy to 2025. This includes publishing by the end of 2025, the updated Q&A documents for qualification of digital heath technologies/AI/ML based methods.

In addition, EFPIA believes that a **flexible risk-based regulatory framework for AI/ML based drug development tools aligned with existing tools and guidelines** (such as the guideline on computerised systems and electronic data modified to include specific considerations for AI systems and tools) **will ensure that terms and requirements for AI will not quickly become outdated**, given the fast pace of evolution in this field. Ultimately this will enable more uptake and adoption of this innovative technology whilst ensuring that regulatory requirements are commensurate with the level of risk posed by the specific AI tool and the context of use.

4. AI policies that balance transparency and protection of innovation when sharing information related to AI models.

Transparency needs to be balanced with the protection of innovation for medicine and technology developers.

EFPIA acknowledges the need for appropriate transparency requirements as they foster trust and can help ensure safety of patients. However, requiring model architecture, logs from modelling, validation and testing, training data and description of the data processing pipeline be submitted as part of a regulatory submission, or publicly disclosed in certain other situations, is not considered proportionate. Furthermore, it may not be possible to provide, or necessary to evaluate the impact of AI on any regulatory decisions, nor needed to ensure the safety of patients.

Such requirements could compromise patient privacy, IP rights, trade secrets and Commercially Confidential Information (CCI) downstream (for example through EMA Policy 0043, Policy 0070 or the Clinical Trials Information System in relation to Clinical Trial Applications (CTA) associated with the AI system). This would **undermine incentives for the pharmaceutical sector to apply AI in research and development in Europe, something currently at risk as highlighted by Mario Draghi's report on European Competitiveness in September 2024**[6] (which, incidentally, calls for guidance on the use of AI in medicines development).

The complexity of this issue is compounded by the fact that sponsors typically work with third parties who consider their underlying code and training data to be a trade secret. IP rights may even be held by the AI developer as a contractor and thus the medicines developer may not have the right to share such information.

EFPIA understands that where the use of AI may impact the benefit-risk evaluation or regulatory decision making, the CTA sponsor, Market Authorisation Applicant (MAA) or the Marketing Authorisation Holder (MAH), may need to provide the scientific rationale along with sufficient

[5] https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance/opinions-letters-support-qualification-novel-methodologies-medicine-development
[6] https://commission.europa.eu/topics/strengthening-european-competitiveness/eu-competitiveness-looking-ahead_en#paragraph_47059

technical details to allow comprehensive assessment of any AI systems used in the medicinal product lifecycle.

In summary, we believe **we can provide sufficient understanding of any AI model without the need to disclose extensive proprietary information in regulatory submissions**. Such a balance could ensure that the EMA/national competent authority has the information needed to assess any impact of AI systems on the benefit-risk assessment of the medicine, whilst retaining AI-related research in medicines development in Europe.

5. Globally aligned regulatory approaches through collaboration among health authorities to foster innovation and support development of safe and efficacious medicines.

EFPIA advocates for **globally aligned, science-driven policy and guidance that promote innovation while ensuring the quality, safety and efficacy of medicines**. Collaboration among regulators is crucial for achieving consistency in this area. It is particularly important to ensure that all d**efinitions, vocabulary and requirements in the AI space are aligned within the EU region and across regions. This will enable the development and application of AI tools** while providing predictability for medicine developers.

The OECD has played a pivotal role by establishing general principles on AI, in addition to a definition of AI systems which was adopted within the EU AI Act, and recently adopted by the EU and US within the Trade and Technology Council meeting vocabulary[7]. This serves as the foundation for forthcoming regulatory guidelines on AI and facilitates global convergence. For this reason, we advocate that the EMA adopts the same definition of an AI system to ensure consistency in AI terminology within the EU.

Similarly, the World Health Organization (WHO) contributes to the healthcare sector by publishing AI-related guidelines[8][9] that serve as a reference for countries looking to establish similar recommendations.

It is important to acknowledge the efforts of the International Coalition of Medicines Regulatory Authorities (ICMRA) in exploring how advancements in AI can support safe and timely access to innovative medicines, as well as foster cross-country collaborations in this field. Under the leadership of EMA, the ICMRA has released a report[10] which includes recommendations to assist regulators in navigating the opportunities and challenges presented by AI. ICMRA has been instrumental in determining the best ways to collaborate and leverage current AI advancements and systems for application in medicine development, thereby facilitating convergence in the field. We encourage further work on AI via ICRMA to continue seeking regulatory convergence.

EFPIA is dedicated to contributing to the **establishment of a common international regulatory understanding of the use of AI in medicines development by bringing related industry experiences and expertise into the process.**

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[7] https://digital-strategy.ec.europa.eu/en/library/eu-us-terminology-and-taxonomy-artificial-intelligence-second-edition

[8] https://www.who.int/news/item/19-10-2023-who-outlines-considerations-for-regulation-of-artificial-intelligence-for-health

[9] https://www.who.int/news/item/18-01-2024-who-releases-ai-ethics-and-governance-guidance-for-large-multi-modal-models

[10] https://www.icmra.info/drupal/sites/default/files/2021-08/horizon_scanning_report_artificial_intelligence.pdf

6. Fostering trust and capability in AI use in medicines R&D through close collaborations among industry, regulators, patients and other stakeholders.

EFPIA believes **collective efforts to build trust and capability in AI systems are needed.** We recommend the following initiatives that can lead to more efficient regulatory processes, spur innovation and ultimately improve patient outcomes:

a) Leverage **existing multi-stakeholders' platforms** such as the planned HMA/EMA multi-stakeholder annual workshop on AI, the ACT EU's platform to facilitate open dialogue and shared learnings (e.g. use cases, best practices), and close collaborations among regulators, industry, and other stakeholders (e.g. patients, academia, industry, data owners, IT vendors, etc.).
b) Design a **dynamic and flexible regulatory framework and processes for AI use in medicines development, proactively engaging all stakeholders**. Consider leveraging existing initiatives, task forces or working groups, e.g. EMA Innovation Task Force, Quality Innovation Group and Methodology Working Party, to promote in-depth technical discussions and enhanced alignment among stakeholders around technical issues including: explainability or transparency, bias and sustainable AI practices; ethical AI development and deployment; lifecycle management of AI models; interoperability and standardization etc.
c) Enhance **access among stakeholders to high quality datasets for training algorithms.** This would include, for example, the European Health Data Space (EHDS). Consider leveraging other EMA data initiatives such as EMA data catalogues.
d) Ensure **appropriate investment in the use of AI in medicines development** through collaborations among public and private sectors.
e) Consider the joint publication of **good principles for the use of AI in the medicines lifecycle in collaboration with other global regulators**. Such principles would set a common baseline understanding of regulatory expectations, including with respect to model training, deployment, and performance. This would mirror ongoing efforts in the medical device area, such as those led by the International Medical Device Regulators Forum (IMDRF) to accelerate international medical device regulatory harmonization and convergence.
f) Consider **leveraging industry best practices on AI compliance/validation** such as the upcoming publication of the International Society for Pharmaceutical Engineering (ISPE) Good Automated Manufacturing Practice (GAMP) AI Good Compliance Guide, which is due to be published in 2025.

EFPIA aims to be a collaborative and constructive partner in shaping this emerging AI policy landscape for medicines and is ready to engage and share our practical experiences that can inform the development of specific guidelines that bring further clarification for the trusted, secure and safe use of AI in the development of medicines.

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Conclusion

EFPIA welcomes the EMA's efforts to support the development and use of AI in the medicines lifecycle, and we encourage continued provision of clarity on its plans and efforts in this field. We seek detailed information from **EMA about how it intends to establish a regulatory framework and implement risk-based approaches for assessments.** It is crucial for EMA to find the right balance between IP and commercially sensitive information protection and appropriate information sharing to facilitate innovation. We encourage EMA to engage in collaborative partnerships with multiple stakeholders to foster knowledge exchange and open dialogues. Moreover, we advocate for global alignment in regulatory approaches towards AI in medicines. Our goal for **AI governance is to have suitable and risk-based guidance for oversight that is tailored to the regulatory status and specific context of use.**

EFPIA would like to underscore the significance of engaging all relevant stakeholders at the highest level in this initiative. We strongly **urge early alignment on establishing a multi-stakeholder platform** to drive the proposal forward, ensuring cooperation among national competent authorities, avoiding fragmentation, and advancing the AI capabilities of Member States.