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EMA Opens Discussion On Appropriate Use Of AI In Drug Lifecycle

by Eliza Slawther

The European Medicines Agency is inviting feedback on a draft reflection paper that outlines the scientific principles companies should follow when using AI tools in the medicinal product lifecycle.

Artificial intelligence (AI) has enormous potential to support the pharmaceutical industry in discovering, developing and marketing medicines, but from a regulatory perspective, this rapidly advancing technology poses unique risks and challenges that must be addressed.

In a 19 July draft *reflection paper* which is open for public consultation until the year-end, the EMA proposes a "human-centric" approach to the use of AI in the medicinal product lifecycle, and advises pharma companies to seek early regulatory support if an AI system is being used in a way that could impact the risk-benefit balance of a drug. It also sets out how companies can prepare documentation for regulators to demonstrate that AI tools have been used in line with good practice guidelines and other relevant principles.

The paper is intended to open a dialogue with drug developers, academics and other regulators "to discuss ways forward, ensuring that the full potential of these innovations can be realized," said Peter Arlett, head of data analytics and methods at the EMA.

AI and machine learning (ML) tools can be used for a vast number of purposes in the drug lifecycle, from selecting trial patients based on certain disease characteristics to supporting data recording and analyses to be used in marketing authorization applications.

"This range of applications brings with it challenges such as the understanding of the algorithms, notably their design and possible biases, as well as the risks of technical failures and the wider impact these would have on AI uptake in medicine development and health," the EMA warns.

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With this in mind, the organization says in its draft paper, it is crucial to identify when and where AI/ML tools fall within the remit of the EMA or member states' national competent authorities because this will impact the level of scrutiny applied to data from these AI tools during assessment processes.

AI/ML Making Inroads In Pharma Industry

AI is already being widely used by the pharmaceutical industry across various stages of drug development. At Roche and its subsidiary Genentech, for example, AI and ML are being applied to "dramatically accelerate and transform" R&D into new therapeutics, diagnostics and treatments, said Tom Brookland, Roche's EU data and AI policy lead in pharma regulatory affairs.

"We believe AI approaches can optimize every single phase of the lifecycle development of a medicine" Brookland told the *Pink Sheet*. "We are advancing the use of AI and ML approaches across the entire lifecycle of medicines development, from early discovery, to pre-clinical, to early and late clinical research and clinical trials, and into the post-approval safety space," he added.

The company said it supported the EMA's efforts to "advance thinking in the critical and rapidly evolving space of AI in medicines." While the reflection paper is just the first step towards developing EU guidance on this topic, Brookland said Roche is keen to join and contribute towards discussions on the use of AI/ML in drug development so that it ultimately results in guidance for industry where none currently exists.

Roche is also preparing a strategy on the responsible and ethical use of AI, he added.

Another company active in this space is Novartis. It is working on a number of initiatives where data science, advanced analytics and AI are being leveraged to augment R&D activities, "from prioritizing compounds for investigation to conducting clinical trials," said a company spokesperson.

"That includes, for example, AI-powered tools designed to empower teams to develop better protocols for clinical trials, and provide key insights for optimization of clinical trial site selection, recruitment and conduct," the firm explained.

Risk Depends On Context

Drug developers should take a risk-based approach to the use of AI and ML tools during all stages of a medical product lifecycle, whereby risks that require management are defined proactively, the EMA paper states.

The agency plans to publish advice on risk management in future guidance, but notes that the degree of risk posed by an AI tool may depend not only on the product itself, but also the context

in which it is used.

Although many factors can contribute to the level of risk posed by using AI in various stages of the drug lifecycle, one of the most important points to consider is the consequences that would arise if the AI product reached an erroneous conclusion in a given context.

In early drug discovery, for instance, a poorly-functioning AI product may result in a molecule being generated that is unviable and does not progress to clinical development. Equally, an AI model may fail to generate any useful drug candidates, resulting in lost resources that could have been used elsewhere.

While both of these situations are sub-optimal, the risk of direct harm to patients when AI is used early on in the development cycle is typically much lower than when it is deployed within a late-stage trial, for instance to determine the dose of an investigational candidate that a patient is given.

Throughout its paper, the EMA stresses that it is the responsibility of companies to identify and systemically manage risks that may arise from using AI or ML tools in any stage of the drug development and post-authorization lifecycle.

Marketing authorization applicants and holders must "ensure that all algorithms, models, datasets, and data processing pipelines used are fit for purpose and are in line with ethical, technical, scientific, and regulatory standards as described in GxP standards and current EMA scientific guidelines," the paper says, which in some cases may be stricter than what is considered standard practice in the field of data science.

Early Regulatory Advice

The EMA also recommends that in cases where the use of an AI/ML system is expected to affect the benefit-risk balance of a medicine, companies should seek early scientific advice or "other early regulatory interaction," such as qualification of innovative development methods for a specific intended use.

The EMA's innovation task force provides early interaction on experimental technology, while scientific advice can be obtained from the Scientific Advice Working Party of the EMA's human medicines committee, the CHMP.

"Timing of interactions should be guided by the regulatory impact and risk associated with using the AI-based models in context of the lifecycle of a medicinal product," the EMA says, which in high-impact cases may be as early as the planning stage.

Companies should prepare documentation for these interactions "at a level of detail sufficient

for comprehensive assessment," and should cover issues such as the intended context of use, the performance and robustness of an AI tool, and its clinical applicability.

Ultimately, the EMA says, the use of AI in the medicinal product lifecycle "should always occur in compliance with the existing legal requirements, by considering ethics and its underlying principles and with due respect of fundamental rights."

The EMA's reflection paper also details specific principles that companies should follow with relation to data protection, AI integrity and trustworthiness, explainability of AI tools and performance assessments.

The draft document was developed as part of the joint Heads of Medicines Agencies and EMA Big Data Steering Group initiative, in liaison with the EMA's CHMP and its Committee for Veterinary Medicinal Products.