

Artificial Intelligence in Pharmaceutical Regulatory Submissions and Approval: A Comparative Review of USFDA and EMA Approaches

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Abstract—The increasing complexity and volume of pharmaceutical regulatory information have created a need for technologies that can support regulatory professionals in preparing, reviewing and managing submissions. Artificial intelligence (AI), including machine learning, natural language processing, generative AI and large language models, is increasingly being explored across the pharmaceutical regulatory lifecycle. AI can assist with regulatory intelligence, regulatory requirement mapping, dossier preparation, electronic Common Technical Document (eCTD) management, submission quality checks, regulatory query management and post-authorization surveillance. However, its use in regulatory activities also raises concerns regarding data quality, model credibility, transparency, bias, confidentiality, cybersecurity, reproducibility and human accountability. The United States Food and Drug Administration (USFDA) issued draft guidance in January 2025 describing a risk-based framework for assessing the credibility of AI models used to support regulatory decisions concerning drug and biological product safety, effectiveness or quality. The European Medicines Agency (EMA) adopted a reflection paper in September 2024 addressing AI and machine learning throughout the medicinal-product lifecycle. In January 2026, FDA and EMA jointly published ten guiding principles for good AI practice in drug development, emphasizing human-centric design, risk-based approaches, context of use, data governance, performance assessment and lifecycle management. This review compares the emerging FDA and EMA approaches and examines practical applications of AI in regulatory submission and approval processes. A human-in-the-loop framework is proposed in which AI supports information processing and analysis while qualified regulatory professionals retain responsibility for interpretation, verification and regulatory decisions. Responsible implementation of AI could improve

efficiency and submission quality while maintaining scientific integrity and patient protection.

Index Terms—Artificial Intelligence; Regulatory Affairs; USFDA; EMA; Regulatory Submission; eCTD

I. INTRODUCTION

The pharmaceutical industry generates a large amount of scientific and regulatory information throughout the development and lifecycle of a medicine. Clinical studies, nonclinical investigations, manufacturing information, quality data, safety reports and administrative documents must be brought together in a structured manner before a product can be submitted to a regulatory authority. Preparing such submissions requires continuous interpretation of regulatory requirements, coordination between departments and careful checking of scientific consistency.

Artificial intelligence (AI) offers an opportunity to support these activities. AI includes machine learning (ML), natural language processing (NLP), generative AI, predictive analytics and robotic process automation. These technologies can process large volumes of structured and unstructured information and identify patterns that may not be immediately apparent during manual review.

FDA has reported increasing experience with AI components in drug-development submissions and has described AI applications across nonclinical, clinical, manufacturing and post-marketing activities. This development indicates that AI is becoming relevant not only to research but also to regulatory evidence generation and assessment.

In January 2025, FDA issued draft guidance on the use of AI to support regulatory decision-making for drugs and biological products. The guidance proposes a risk-based credibility assessment framework linked to a defined context of use. EMA adopted its reflection paper on AI in the medicinal product lifecycle in September 2024, covering AI and ML applications from drug discovery through post-authorisation activities [1] [2].

In January 2026, FDA and EMA jointly published ten guiding principles for good AI practice in drug development. These principles include human-centric design, risk-based approaches, clear context of use, multidisciplinary expertise, data governance, model development, performance assessment and lifecycle management.

The objective of this review is to examine the role of AI in pharmaceutical regulatory submissions and approval, compare the emerging approaches of USFDA and EMA, identify opportunities and limitations, and propose a human-in-the-loop framework for responsible implementation.

II. REVIEW METHODOLOGY

This article was prepared as a narrative review and comparative analysis of regulatory documents and scientific literature concerning AI in pharmaceutical regulatory affairs. Official FDA and EMA documents were prioritized for regulatory statements, while selected peer-reviewed literature was used to provide scientific context. The review focused on AI applications in regulatory intelligence, submission preparation, eCTD management, regulatory review, regulatory decision support, governance and lifecycle management.

III. AI IN PHARMACEUTICAL REGULATORY AFFAIRS

AI is relevant to regulatory affairs because the discipline involves large volumes of documents, structured data and changing regulatory requirements. NLP can support regulatory document searching, classification, terminology checking and requirement extraction. Machine learning can support pattern recognition, prediction and prioritization. Generative AI can assist with preliminary summaries

and drafting, while robotic process automation can handle repetitive workflow tasks.

The value of AI is therefore greatest when it reduces repetitive information-processing activities while allowing qualified regulatory professionals to retain responsibility for interpretation and final decisions .

IV. AI IN REGULATORY INTELLIGENCE AND REQUIREMENT MAPPING

Regulatory intelligence involves collecting, interpreting and communicating information about regulatory requirements and developments. AI can monitor regulatory guidance, agency announcements, assessment reports, safety communications and scientific publications. It can then identify potentially relevant changes and map them to products, markets or submission activities.

A practical workflow is: Regulatory Sources → AI Monitoring → Information Extraction → Requirement Identification → Impact Assessment → Human Review → Regulatory Action.

AI can also help construct regulatory requirement matrices by linking requirements to CTD modules and supporting evidence. However, an AI-identified gap should be treated as an alert requiring human verification rather than as a final regulatory conclusion.

V. AI IN REGULATORY DOSSIER PREPARATION AND eCTD MANAGEMENT

AI can assist with document summarization, data extraction, terminology checking, consistency checking, cross-reference verification, document classification and identification of potentially missing information. For example, an AI system could compare study identifiers, patient numbers, dates or endpoints across protocols, clinical study reports and CTD sections.

AI can also support eCTD management by classifying documents, extracting metadata, identifying broken hyperlinks and duplicate documents, and assisting with lifecycle tracking. Such tools may improve submission readiness by identifying technical and content-related issues before a dossier is submitted.

At the marketing-authorisation stage, EMA has specifically identified potential AI applications such

as drafting, compiling, translating and reviewing information intended for product information, while also recognizing the associated risks and need for human-centric implementation .

VI. AI IN REGULATORY REVIEW AND APPROVAL

Regulatory agencies can potentially use AI for information retrieval, document summarization, cross-document comparison, pattern identification and support for regulatory questions. AI may help reviewers navigate very large submissions more efficiently, but these applications should be regarded as decision-support tools rather than autonomous decision-makers.

FDA's 2025 draft guidance is particularly relevant when AI-generated information is intended to support a regulatory decision concerning drug or biological-product safety, effectiveness or quality. The guidance emphasizes that the credibility of an AI model should be evaluated for its particular context of use and according to the risk associated with that use.

VII. USFDA APPROACH

FDA's January 2025 draft guidance, 'Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products,' proposes a risk-based credibility assessment framework for AI models used to generate information intended to support regulatory decisions . The framework is centered on context of use (COU), meaning the specific role and purpose for which an AI model is used.

A low-risk application might involve summarizing a publicly available regulatory document. A more consequential application might identify inconsistencies across a regulatory dossier. A high-risk application could involve AI-generated evidence that contributes to conclusions about safety or effectiveness. The level of credibility assessment

should therefore be proportionate to the intended use and risk .

FDA also identifies AI as an area of continuing development in drug regulation and research, including the responsible use of AI within regulatory, scientific and administrative activities [4].

VIII. EMA APPROACH

EMA's Reflection Paper on the Use of Artificial Intelligence in the Medicinal Product Lifecycle was adopted in September 2024. It addresses AI and ML applications across the lifecycle of human and veterinary medicines, from discovery and development through manufacturing, authorization and post-authorisation activities .

EMA emphasizes human-centric use, scientific validity, data quality, transparency, data protection and compliance with applicable legal requirements. Where an AI/ML system may affect the benefit-risk balance of a medicine, early regulatory interaction is encouraged.

EMA's broader AI strategy also includes development of tools, regulatory guidance, collaboration and experimentation to strengthen the European medicines regulatory network's ability to use and oversee AI, [5].

IX. FDA–EMA CONVERGENCE

The January 2026 FDA–EMA Guiding Principles of Good AI Practice in Drug Development represent an important step toward international convergence. The ten principles are: (1) human-centric by design; (2) risk-based approach; (3) adherence to standards; (4) clear context of use; (5) multidisciplinary expertise; (6) data governance and documentation; (7) model design and development practices; (8) risk-based performance assessment; (9) lifecycle management; and (10) clear, essential information.

These principles provide a common foundation for responsible AI use while allowing implementation within different legal and regulatory frameworks .

X. COMPARATIVE ANALYSIS OF USFDA AND EMA

Parameter	USFDA	EMA
Major AI document	2025 draft guidance	2024 reflection paper
Primary focus	AI supporting regulatory decision-	AI across medicinal-product

	making	lifecycle
Key concept	Context of Use and model credibility	Human-centric lifecycle approach
Risk assessment	Strong emphasis	Strong emphasis
Human oversight	Essential	Essential
Data governance	Important	Important
Model performance	Credibility assessment	Performance and scientific validity
Lifecycle management	Increasingly emphasized	Explicitly addressed
Regulatory interaction	Important	Encouraged
International cooperation	Joint FDA–EMA principles	Joint FDA–EMA principles

XI. GENERATIVE AI IN REGULATORY AFFAIRS

Generative AI is particularly relevant because it can create summaries, draft text and answer questions from largedocument collections. In regulatory affairs, possible applications include preliminary document drafting, regulatory summaries, gap-analysis reports, meeting summaries and preparation of draft responses to regulatory questions [8].

However, generative AI may produce plausible but incorrect statements, unsupported citations or inconsistent outputs. Therefore, confidential regulatory information should be processed only within appropriately governed environments, and every substantive AI-generated output should be checked against authoritative source documents.

The FDA–EMA principles support a risk-based and human-centric approach, including clear context of use, data governance, performance assessment and lifecycle management .

XII. PROPOSED HUMAN-IN-THE-LOOP REGULATORY AI MODEL

A human-in-the-loop model is proposed for pharmaceutical regulatory submissions. The workflow is: Regulatory Question → Define Context of Use → Risk Assessment → Data Assessment → AI Tool Selection → Model Performance Evaluation → AI Output → Human Expert Verification → Quality/Regulatory Review → Approved Regulatory Information → Submission or Regulatory Decision → Continuous Monitoring.

The central principle is that AI provides analysis and information-processing support, while qualified professionals provide scientific interpretation, regulatory judgment and accountability. This is consistent with the human-centric principles jointly articulated by FDA and EMA .

XIII. AI APPLICATION–RISK–CONTROL FRAMEWORK

AI application	Potential benefit	Potential risk	Recommended control
Regulatory document search	Faster retrieval	Low	Source verification
Document summarization	Time saving	Low–moderate	Human review
Gap analysis	Improved readiness	Moderate	Expert verification
eCTD quality checks	Error detection	Moderate	Technical validation
Regulatory response drafting	Faster preparation	Moderate	SME approval
Safety signal detection	Early signal identification	High	Validated model
Clinical prediction	Decision support	High	Credibility assessment
Efficacy prediction	Evidence support	High	Scientific validation

XIV. BENEFITS OF AI

The major potential benefits include improved efficiency, reduced repetitive work, faster regulatory

intelligence, more consistent document checking, improved submission readiness and better knowledge management. AI may allow regulatory professionals to spend more time on scientific interpretation and strategic decision-making.

XV. CHALLENGES AND LIMITATIONS

Major challenges include data quality, algorithmic bias, hallucination in generative AI, limited explainability, confidentiality, cybersecurity, model drift, reproducibility, validation and accountability. The credibility of an AI model must be considered in relation to its intended use rather than assumed solely from general model performance [9].

Regulatory submissions may contain confidential commercial information, so organizations should establish appropriate controls for data access, model deployment, audit trails and output review. AI systems should also be monitored throughout their lifecycle because software, data and model performance can change.

XVI. HUMAN OVERSIGHT AND REGULATORY ACCOUNTABILITY

AI should not replace qualified regulatory, scientific or clinical judgment. Instead, responsibility should be divided clearly. AI can retrieve information, generate preliminary summaries, identify possible gaps and flag inconsistencies. Human experts should verify evidence, assess scientific significance, determine regulatory strategy and approve final submission content.

This approach is consistent with the FDA–EMA emphasis on human-centric design and multidisciplinary expertise.

XVII. FUTURE PERSPECTIVES

Future regulatory systems may include AI-enabled eCTD quality control, regulatory knowledge graphs, secure regulatory AI assistants, automated cross-jurisdiction requirement mapping and AI-supported pharmacovigilance. AI may also increasingly complement model-informed drug development. FDA's current AI and drug-development activities indicate that the regulatory environment is moving toward structured, risk-based and evidence-focused approaches to AI [10].

International convergence is also likely to increase. The joint FDA–EMA principles provide a foundation for further development of common good practices and consensus standards.

XVIII. RESEARCH GAP AND FUTURE RESEARCH DIRECTIONS

Further empirical research is required to determine whether AI actually reduces regulatory submission preparation time, decreases deficiencies, improves document consistency and maintains or improves reviewer accuracy. Controlled studies comparing human-only, AI-assisted and human-plus-AI workflows would be particularly valuable.

Research is also needed on validation methods for generative AI, hallucination rates in regulatory applications, reproducibility of AI outputs, governance of confidential regulatory data and standardized approaches for documenting AI model performance.

XIX. DISCUSSION

The use of AI in pharmaceutical regulatory affairs is developing at a time when regulatory agencies themselves are exploring AI-enabled tools. This creates a shift from viewing AI only as a technology used by industry toward considering AI as part of the broader regulatory ecosystem.

The FDA's context-of-use approach provides a practical mechanism for determining how much evidence is needed to establish AI model credibility for a particular regulatory purpose. EMA's lifecycle approach complements this by considering AI from discovery through post-authorisation use. The joint 2026 principles further indicate convergence around human-centric design, risk-based implementation, data governance, performance assessment and lifecycle management.

Generative AI is likely to be useful for information-intensive regulatory activities, but its outputs must be verified because fluency does not guarantee factual accuracy. The future regulatory professional is therefore more likely to work with AI as a co-pilot than to be replaced by it.

XX. CONCLUSION

Artificial intelligence has considerable potential to improve pharmaceutical regulatory submission and approval processes. Its applications range from regulatory intelligence and dossier preparation to eCTD management, submission quality control,

regulatory review, regulatory correspondence and post-authorisation surveillance.

The USFDA and EMA have both recognized the importance of responsible AI implementation. FDA's 2025 draft guidance provides a risk-based framework for assessing AI model credibility when AI supports regulatory decisions involving drug or biological-product safety, effectiveness or quality. EMA's 2024 reflection paper addresses AI throughout the medicinal-product lifecycle and emphasizes human-centric implementation, scientific validity, data quality and lifecycle considerations.

The joint FDA–EMA principles published in January 2026 provide an important step toward international convergence. The most appropriate model is therefore not AI → regulatory decision, but AI → analysis and evidence → human verification → regulatory decision.

Responsible adoption of AI will depend on reliable data, clear context of use, appropriate risk assessment, model validation, traceability and meaningful human oversight. AI should therefore be viewed as a regulatory co-pilot that strengthens the capabilities of regulatory professionals while preserving scientific integrity, accountability and patient protection.

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DECLARATION OF GENERATIVE AI USE

Generative AI tools were used during manuscript preparation for language refinement, organization of sections and drafting assistance. The author independently reviewed, verified and edited the scientific and regulatory content and remains responsible for the accuracy, interpretation and final version of the manuscript.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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