Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 191 - 192 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.091
Short communication

Artificial Intelligence in clinical trials – ethical and regulatory considerations

Cvetanka Trpenoska[1,2 *], Kristina Mladenovska[2]

[1]*Comac Medical Ltd, St Georgi Skrizevski No 6B, 1000 Skopje, Republic of N Macedonia*
[2]*Faculty of Pharmacy, University Ss Cyril and Methodius in Skopje, Blv. Mother Theresa, No 45, 1000 Skopje, Republic of N Macedonia*

Introduction

Today's pharmaceutical industry is facing a critical challenge as traditional research and development methods become increasingly unsustainable. This phenomenon, known as Eroom's Law, refers to the rising costs and declining efficiency of drug development. Developing a new drug can take 10–15 years and cost more than 2 billion USD, while only about 10% of drugs entering clinical trials ultimately gain approval. In this context, artificial intelligence (AI) offers significant potential to accelerate drug development, reduce costs, and improve patient access to life-saving therapies. AI integration fundamentally transforms clinical research by optimizing trial design, recruitment, data analysis, and digital patient monitoring. However, its rapid adoption in a highly regulated industry raises ethical and regulatory concerns, requiring effective frameworks to safeguard scientific integrity and patient safety.

The role and impact of AI on clinical trials

The transformative potential of AI is particularly evident in the optimization of clinical trial protocols and patient recruitment. By analyzing historical and real-world data (RWD), AI improves inclusion criteria, enhances statistical power, reduces costs, and accelerates recruitment. Since over 80% of clinical trials face delays due to difficulties in finding suitable participants, AI-powered natural language processing (NLP) systems can analyze electronic health records and accurately match patients with trial requirements. This enables more precise participant selection, leading to smaller and more efficient trials with improved statistical reliability. In addition, digital health technologies (DHTs) support the transition from traditional to decentralized clinical trials. Through sensor-derived digital biomarkers, AI enables real-time, remote patient monitoring and early adverse event detection. Consequently, AI-driven trials become more efficient, cost-effective, and less burdensome for participants.

Machine learning

Machine Learning (ML) identifies complex patterns in large, heterogeneous datasets without explicit programming. Unlike traditional statistical methods, ML efficiently processes high-dimensional data, such as genomic information and continuous sensor outputs. Its applications are generally divided into three main approaches. Supervised learning uses labeled data for patient screening and recruitment based on treatment response or risks. Unsupervised learning analyzes unlabeled data to identify hidden structures like new disease subgroups. Deep Learning (DL) effectively analyzes medical images and longitudinal device data. However, despite their

*c.trpenoska@gmail.com

strong predictive capabilities, DL models often function as "black boxes," creating challenges for transparency and regulatory approval, which has increased the importance of explainable AI (XAI).

The role of AI in pharmacovigilance during clinical trials

The application of AI and ML in pharmacovigilance improves drug safety monitoring by enabling real-time risk assessment, faster detection of adverse events, and more efficient analysis of clinical trial data. Technologies such as ML, NLP and XAI enhance transparency, safety, and regulatory compliance while supporting, rather than replacing, human expertise (CIOMS, 2025). With their help, precise MedDRA coding, triage of serious adverse events, and predictive toxicology through sophisticated *in-silico* modeling are enabled.

Challenges and limitations of AI in clinical trials

AI in clinical trials faces key challenges including poor-quality and unrepresentative data, which can lead to bias, and the "black box" problem, which reduces trust due to lack of transparency. These issues may also threaten health equity when models perform poorly for underrepresented groups. Overcoming them requires XAI, stronger privacy protection, model auditing, and clear regulatory standards for accountability (Lovejoy et al., 2022).

Regulatory frameworks for AI in clinical trials

Regulatory frameworks for AI in clinical trials are evolving through two main approaches: the flexible, risk-based model of the U.S. Food and Drug Administration (FDA) and the legally binding framework of the European Medicines Agency (EMA) supported by the EU AI Act. The FDA emphasizes early collaboration with sponsors and evaluates AI models according to their "context of use" and impact on study endpoints, encouraging flexible integration of AI in clinical research. (U.S. FDA, 2025). In contrast, the European approach prioritizes transparency, human oversight, and strict data protection. Under the EU AI Act, higher-risk AI systems face stricter requirements for validation and accountability, meaning that algorithms used in clinical trials must undergo rigorous evaluation similar to pharmaceutical products themselves (Regulation (EU) 2024/1689). Other countries, such as the United Kingdom and Canada, also promote responsible AI integration through ethical guidelines, regulatory oversight, and clinical validation requirements. Globally, standards such as GMLP, SPIRIT-AI, and CONSORT-AI aim to establish unified principles for the safe and ethical use of AI in the pharmaceutical industry.

Conclusion

The integration of AI into clinical trials has the potential to transform medical research by improving trial design, patient recruitment, data analysis, and monitoring. Technologies such as ML, DL, and NLP can make clinical trials more efficient, personalized, and patient-centered. However, challenges such as poor data quality, algorithmic bias, lack of transparency, and evolving regulatory requirements remain significant concerns. The successful use of AI will require collaboration between researchers, clinicians, regulators, and patients to ensure ethical, transparent, and safe implementation in clinical research.

References

CIOMS, 2025. Artificial intelligence in pharmacovigilance (Draft). CIOMS-WG-XIV_Draft-report-for-Public-Consultation_1May2025. https://cioms.ch/wp-content/uploads/2022/05/CIOMS-WG-XIV_Draft-report-for-Public-Consultation_1May2025.pdf

Lovejoy, C.A. et al., 2022. Key considerations for the use of artificial intelligence in healthcare and clinical research. Future Healthc. J. 9(1), 75-78. https://doi.org/10.7861/fhj.2021-0128

Regulation (EU) 2024/1689 of the European Parliament and of the Council of 13 June 2024 laying down harmonised rules on artificial intelligence (Artificial Intelligence Act). https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202401689

U.S. FDA., 2025. Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products. Guidance Document. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-artificial-intelligence-support-regulatory-decision-making-drug-and-biological