How Does the FDA Evaluate AI in Combination Products?

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Published: March 22, 2015 | FDA Regulation and Compliance

DOI: 10.5281/zenodo.17999369

Abstract

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Introduction

The integration of Artificial Intelligence (AI) into combination products, which merge a drug, device, and/or biological product, is rapidly transforming the healthcare landscape. These AI-enabled combination products offer immense potential for personalized medicine, improved diagnostics, and enhanced therapeutic outcomes. However, their unique characteristics, particularly the adaptive nature of AI algorithms, present significant challenges for regulatory bodies like the U.S. Food and Drug Administration (FDA). This article explores how the FDA evaluates AI in combination products, focusing on the current regulatory framework, emerging strategies, and the challenges that lie ahead.

The FDA's Regulatory Framework: A Balancing Act

The FDA's approach to regulating AI in combination products is a delicate balancing act between fostering innovation and ensuring patient safety and product effectiveness. The agency primarily relies on its existing risk-based framework for medical devices, including the 510(k) premarket notification, De Novo classification, and Premarket Approval (PMA) pathways [1]. However, the dynamic and adaptive nature of AI algorithms, which can learn and evolve from real-world data, challenges the traditional, static nature of these regulatory pathways.

A key component of the FDA's strategy is the concept of a **Predetermined Change Control Plan (PCCP)**. A PCCP is a plan that a manufacturer submits to the FDA as part of a premarket submission. It describes the anticipated

modifications to an AI/ML-based Software as a Medical Device (SaMD), including changes to its performance, inputs, or intended use. The goal of a PCCP is to allow manufacturers to make certain modifications to their AI algorithms without needing to submit a new regulatory submission for each change, as long as the changes are within the scope of the approved PCCP [2]. This approach provides a degree of flexibility for manufacturers to improve their products while maintaining regulatory oversight.

Navigating the Challenges of AI Evaluation

Despite the development of frameworks like the PCCP, several challenges remain in the evaluation of AI in combination products. The traditional 510(k) pathway, which relies on demonstrating “substantial equivalence” to a legally marketed predicate device, is not well-suited for adaptive AI algorithms that are designed to continuously learn and evolve. The dynamic nature of these algorithms makes it difficult to establish a fixed point of comparison, creating a regulatory hurdle for manufacturers [3].

Furthermore, AI models are trained on large datasets, and if these datasets are not representative of the intended patient population, they can perpetuate and even amplify existing biases. The performance of AI models can also degrade over time as they encounter new data in the real world, a phenomenon known as “model drift.” This can lead to inaccurate or unreliable outputs, posing a risk to patient safety [3]. The “black box” nature of some complex AI algorithms can also make it difficult for regulators and clinicians to understand how they arrive at their conclusions, posing a challenge for evaluating the safety and effectiveness of these devices and for building trust among users. Finally, the emergence of state-level AI legislation adds another layer of complexity for manufacturers to navigate [2].

The FDA's Emerging Strategies for a New Era of AI

To address these challenges, the FDA is actively developing and refining its regulatory approach to AI in combination products. The agency is engaging with stakeholders through public workshops, guidance documents, and programs like the Emerging Drug Safety Technology Meeting (EDSTM) to foster collaboration and mutual learning [3]. A cornerstone of this evolving strategy is the adoption of a **Total Product Lifecycle (TPLC) Approach**. This approach involves a continuous process of monitoring and evaluation from pre-market development to post-market performance, which is better suited to the iterative nature of AI.

In line with the TPLC approach, the FDA is increasingly focused on leveraging real-world data and evidence to monitor the performance of AI-enabled devices after they are on the market. This allows the agency to identify and address potential issues, such as model drift and data bias, in a timely manner. The FDA is also collaborating with other regulatory bodies, both domestically and internationally, to harmonize regulatory requirements for AI in medical devices, which will help to create a more predictable and efficient regulatory environment for manufacturers.

Conclusion

The evaluation of AI in combination products is a complex and evolving area of regulation. The FDA is taking a proactive and adaptive approach, working to balance the need for innovation with the imperative of patient safety. While challenges remain, the agency's focus on a total product lifecycle approach, real-world performance monitoring, and collaboration with stakeholders provides a promising path forward. As AI technology continues to advance, it is crucial for manufacturers, regulators, and clinicians to work together to ensure that these innovative products are developed and deployed in a safe, effective, and ethical manner.

References

[1] U.S. Food and Drug Administration. (n.d.). *Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices*. FDA. Retrieved from https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

[2] Al-Faruque, F. (2025, November 19). *Experts: PCCPs can advance AI in combination products, be aware of state laws*. RAPS. Retrieved from https://www.raps.org/news-and-articles/news-articles/2025/11/experts-pccps-can-advance-ai-in-combination-produc

[3] Santra, S., Kukreja, P., Saxena, K., Gandhi, S., & Singh, O. V. (2024). Navigating regulatory and policy challenges for AI enabled combination devices. *Frontiers in Medical Technology*, *6*. https://doi.org/10.3389/fmedt.2024.1473350