National Coordination Office
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Request for Information on the Development of an Artificial Intelligence (AI) Action Plan

Ensuring Efficient and Innovative Regulatory Approaches for AI in Drug Development

The integration of Artificial Intelligence (AI) and Machine Learning (ML) into drug development and diagnostics presents unprecedented opportunities to enhance patient care, streamline drug discovery, and improve the accuracy of diagnosis and treatment selection. However, these technologies may require a new regulatory paradigm, particularly given their adaptive nature. To ensure safety, efficacy, and reliability, regulatory frameworks must evolve to accommodate AI-driven innovations while maintaining robust oversight mechanisms.

This comment outlines key considerations for regulatory oversight and policy development to support the safe and effective integration of AI/ML technologies into drug development, leveraging lessons learned from ongoing pilot projects focused on computational pathology and diagnostics.[1] These recommendations align with the goals of the AI Action Plan by providing structured policy actions that promote AI innovation while ensuring regulatory clarity and patient safety.

Key Considerations for AI in Drug Development

1. Adapting FDA Regulatory Pathways for AI/ML Platforms

Given the dynamic nature of AI/ML models, novel regulatory approaches should account for their continuous learning and evolving capabilities. Potential actions include:

- **Risk-Based Regulatory Framework:** FDA should implement a risk-based approach tailored to the intended use of AI-based platforms. A flexible yet structured framework will ensure that regulatory expectations align with patient-centered benefit-risk considerations.

[1] Brittany McKelvey, et al. Agreement Across 10 Artificial Intelligence Models in Assessing HER2 in Breast Cancer Whole Slide Images: Findings from the Friends of Cancer Research Digital PATH Project. San Antonio Breast Cancer Conference Abstract. https://friendsofcancerresearch.org/wp-content/uploads/SABCS-Poster_Digital-PATH-Project-Findings.pdf

- **Clarifying Regulatory Expectations:** FDA guidance should explicitly define the evidence required for AI-based tools in oncology clinical trials, including computational pathology and biomarker evaluation.
- **Prospective Criteria for AI Validation:** Establishing predefined performance criteria and validation standards can support the rapid and safe deployment of AI in clinical decision-making.

2. Developing Expedited Validation Processes using Reference Data Sets

Reliable and standardized datasets are essential for AI model validation and regulatory assessment. Reference datasets can:

- Support model comparability across different AI-based tools, similar to how biomarker assays are validated.
- Enable independent validation, ensuring AI models perform consistently in the intended use population.
- Reduce variability in AI-based tools, enhancing regulatory decision-making and clinical adoption.

As outlined in the Friends of Cancer Research Digital PATH Project, publicly available reference datasets can provide a benchmark for efficiently assessing AI performance.[2] These datasets should be representative of all populations and include critical metadata such as clinical characteristics, image acquisition details, and biomarker distributions. Such an approach would be substantially more efficient than current requirements, in which individual validation processes would need to be constructed for each tool.

3. Defining Performance Metrics and Standards

To ensure AI-based diagnostic and prognostic tools are reliable and reproducible, standardized performance metrics are necessary. Regulatory actions should include:

- **Analytical Validation:** AI models should undergo accuracy, precision, and interchangeability assessments to ensure reliability across different settings.
- **Clinical Validation:** AI-driven diagnostics should demonstrate clinical validation through well-defined sensitivity, specificity, and treatment-response predictions, when appropriate.

[2] Friends of Cancer Research Discussion Document: Considerations for Developing Reference Data Sets for Digital Pathology Biomarkers. https://friendsofcancerresearch.org/wp-content/uploads/Considerations-for-Developing-Reference-Data-Sets-for-Digital-Pathology-Biomarkers-.pdf

- **Regulatory Harmonization:** Collaboration between regulatory agencies, industry leaders, academic researchers, and patient advocates can help align performance expectations for AI-driven drug development.

Policy Actions and Opportunities

To facilitate the integration of AI/ML into regulatory pathways, several opportunities are noted:

- **Establish a Clear AI Regulatory Framework:** Develop specific guidance for the use of AI in clinical research and care, detailing expectations for data quality, validation, and clinical evidence generation.
- **Develop an Expedited Validation Pathway:** Support initiatives that generate non-proprietary reference datasets to facilitate independent validation of AI models and enhance regulatory review efficiency.
- **Implement Adaptive Regulatory Mechanisms:** Advance adaptive regulatory mechanisms that enable iterative AI model updates based on real-world data, aligning with established approaches for Software as a Medical Device (SaMD).
- **Encourage Cross-Sector Collaboration:** Strengthen partnerships among regulatory agencies, industry leaders, and academic institutions to establish best practices for AI-driven diagnostics and digital pathology applications.

Conclusion

AI and ML hold immense potential to revolutionize drug development and patient care. However, realizing their full benefits requires regulatory policies that balance innovation with rigorous oversight. By establishing robust reference datasets, defining clear performance metrics, and developing adaptive regulatory frameworks, stakeholders can work together to ensure AI technologies are safely and effectively integrated into the future of precision medicine and oncology drug development.

We appreciate the opportunity to contribute to this Request for Information and look forward to working collaboratively with policymakers to consider these recommendations in developing an AI Action Plan that promotes both innovation and patient safety.

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Sincerely,

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