PERSONALIZED MEDICINE COALITION

April 7, 2025

Dockets Management Staff
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Considerations for the Use of Artificial Intelligence to Support Regulatory Decision Making for Drug and Biological Products [FDA-2024-D-4689]

To Whom It May Concern:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 200 institutions from across the health care spectrum, thanks the U.S. Food and Drug Administration (FDA) for the opportunity to submit comments related to the draft guidance titled *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision Making for Drug and Biological Products*.[i] PMC believes that emerging and potential uses of AI may begin to improve patient experiences with health care and help address challenges to the clinical adoption of personalized medicine.[ii] PMC applauds the FDA for recognizing opportunities for AI to produce information or data intended to support regulatory decision-making regarding safety, effectiveness, or quality for drugs and biologic products. Furthermore, we appreciate the Agency's efforts to establish a risk-based credibility assessment framework that may be used for establishing and evaluating the credibility of an AI model for a particular context of use.

Personalized medicine is a rapidly evolving field in which physicians use diagnostic tests and individual details about a person and their health to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients.

Personalized medicine is helping to shift the patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions, which leads to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. PMC and its members are leading the way in personalized medicine and in developing evidence showing how patients and the health care system can benefit from appropriate testing and tailored treatment as soon as possible during their clinical experiences.

Statement of Neutrality

PMC's members may present their own responses to the FDA's draft guidance titled *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision Making for Drug and Biological Products* and actively advocate for those positions. PMC's response is designed to provide feedback so that the general concept of personalized medicine can advance, and is not intended to impact adversely the ability of individual PMC members, alone or in combination, to submit separate responses to FDA on this draft guidance.

PMC advocates for public policies that can help AI realize its full potential for improving patient access to personalized medicine and for making the health care system more efficient across disease areas. The following comments share our observations on challenges in AI development and use. They also highlight relevant recommendations from PMC's *Policy Principles on AI*, developed in collaboration with PMC's AI Working Group. We encourage the FDA to incorporate these recommendations in finalizing this guidance and when developing any future guidance documents relevant to AI tools that support personalized medicine.

I. Challenges in the Development and Use of AI

AI has applications in pre-clinical and clinical settings. We appreciate that the Agency has reflected some of these applications as examples in the draft guidance for their benefits to regulatory decision-making, such as the integration of data from various sources for clinical evidence generation; processing and analyzing large sets of data (e.g. digital health technologies (DHTs) and real-world data (RWD)); and facilitating reporting of post-market adverse event experience information. PMC's focus is on ensuring the right regulatory framework for AI is used throughout the drug and biological lifecycle, from evidence generation and commercialization, to use by patients and doctors to make health care decisions. In developing frameworks for regulatory oversight, certain cross-cutting policy challenges will need to be considered. In the draft guidance, FDA acknowledges some of the challenges with AI that we face with respect to its development and use in supporting personalized medicine.

Regulatory Oversight Challenges

AI tools rely on large amounts of data from various sources. As noted by FDA in the draft guidance, these data sources can vary in their quality and representativeness. When AI algorithms are neither created nor validated using the same dataset, this creates challenges for regulatory bodies like the FDA to compare and consistently evaluate tools. The sensitivity of an AI tool may not be comparable across applications, and AI models can have differing levels of explainability, or transparency into the reasoning behind the model's output. This lack of standardization can complicate and lead to inconsistencies in regulatory oversight, since it is difficult to establish clear benchmarks for AI performance across different applications. To facilitate predictable regulatory oversight and build trust in the quality of AI technologies when used in real-world clinical settings, collaborative efforts are needed to create comprehensive and standardized datasets – representative of all patient populations – for training and validating AI algorithms, including tests for biases that could impact real-world implementation across different health care settings.

Also noted in the draft guidance is that for some AI tools, the technology's training data and decision-making process can be opaque. Training data must be reflective of the intended population and product

developers must take steps to address bias and account for limitations in health data throughout the product's lifecycle. Clear regulatory processes and frameworks that establish or clarify technical standards for the quality and representativeness of training data, result reporting, data governance, data sharing, data privacy, data security, transparency, bias mitigation, and informed consent where required will be essential to set consistent expectations for developers and build trust among providers and patients in the real-world use of AI. Real-world monitoring can also help track biases and other issues that may emerge with implementation of AI, as well as document benefits that could support broader implementation.

Real-World Implementation Challenges

Human-related biases and biased data can seep into AI algorithms during deployment that lead to treatment recommendations that are inaccurate. AI models should be designed to mitigate algorithmic bias throughout their product lifecycle. Since AI can come to false conclusions, AI tools should be used to support, and not supplant, human decision-making. Human oversight, transparency in how and when AI algorithms are used, and other bias mitigation strategies can help ensure health care decisions appropriately reflect individual patients' needs and preferences.

AI applications are also more likely to be implemented in large, well-resourced academic medical centers. Considering how the implementation of AI technologies can be made more accessible regardless of geography and facility type would help avoid exacerbating existing health care access barriers. Studies generating best practices or evidence on the value of integrating AI can collectively help realize its full potential for improving patient access to personalized medicine. Public-private collaborations can also aid in developing solutions for integrating and maximizing the use of AI across disease states, patient populations, and health care settings.

II. Recommendations for Regulatory Oversight of the Use of AI in Regulatory Decision-Making for Drugs and Biologics

There are many use cases for AI in health care relevant to personalized medicine. Experts in PMC's AI Working Group identified multiple use cases for AI to advance clinical research and the development of medical products. AI may:

- support faster identification and assessment of novel measures, biomarkers, or clinical endpoints;
- inform enhanced statistical analysis and study design options; screen or pre-screen patients more efficiently;
- collect, manage, and analyze data, such as genomic, imaging or other information; RWD; data from DHTs; or in silico clinical trials, in ways that support enrichment strategies; and
- improve the experience of trial participants to promote retention and representativeness, such as through DHTs, decentralized trials, or enhanced methods for participants to receive information about a study.

The scope of this draft guidance does not address important uses of AI to support personalized medicine, such as AI's use in drug discovery and to achieve operational efficiencies that do not impact patient safety, drug quality, or the reliability of results from nonclinical and clinical studies. Regulatory oversight of AI will ensure confidence in the performance and use of AI and mitigate risks to patients at each step in the drug and biologic development process while continuing to foster innovation.

FDA should maintain an appropriate risk-based and flexible approach that ensures predictability. Regulatory frameworks should ensure AI models are trained on appropriately validated data by specifying technical standards for the quality and comprehensiveness of training data, standards to improve the comparability of reported results, and be comprehensive enough to apply to various use cases. In developing a risk-based framework for oversight, regulators should consider differing levels of explainability in how AI models arrive at their outputs. Regulators should also allow adaptive regulatory approaches that allow for iterative development and continuous improvement of AI-based tools and technologies. In this context, the Agency could clarify when an AI use case is subject to regulatory review and provide optimal strategies for engaging with the FDA to receive feedback on model uses.

To assess potential benefits and risks to patients comprehensively, regulatory oversight should consider a product's **total product lifecycle**. This approach could include the use of real-world monitoring to identify and address issues or challenges that may emerge with implementation of AI, as well as identify realized benefits that could expand a product's utility and permissible uses. **For those sponsors with AI tools who seek qualification of the tool as envisioned in the draft guidance, the guidance includes lifecycle maintenance and post-approval change management planning as a starting point. The guidance should further identify opportunities within the change management planning process for developers to receive prospective input from the Agency.**

AI-enabled medical products often rely on cloud-based infrastructure, networked environments, and integration with electronic health record systems—introducing potential vulnerabilities to data breaches, unauthorized access, and manipulation of algorithmic functions. Because AI-enabled tools may interact with live clinical systems and continuously learn or update over time, ensuring secure and trustworthy system operation is essential to protecting patient safety. **To facilitate trust and accountability over how AI is developed and deployed for personalized medicine purposes, prescribed processes regarding the use, disclosure, confidentiality, integrity, and availability of patient data should be transparent and robust.** This can include, for example, considerations for how to obtain informed consent when it is required; clarification of when it is not required; how to securely transfer individuals' personal health information with encryption; and how to mitigate threats to cybersecurity and data integrity. **Clarity in data governance and interoperability for AI tools and technologies is also needed to help scale and facilitate their use in stratifying patients for personalized medicine. The draft guidance does not address steps developers can take to ensure human subject protection or cybersecurity.**

Ensuring that AI tools perform consistently in different clinical contexts and across a broad array of patient populations is vital to maintaining patient safety and reliable health outcomes. Although AI holds promise, inconsistencies in real-world performance have been observed. **To help mitigate biases in AI, developers and regulators should prioritize efforts to ensure training data is reflective of the intended population and account for shortcomings in health data** throughout the product development lifecycle. AI algorithms should be transparent in the data they are trained on, and regulators should test for biases that could impact their real-world implementation. **For developers who seek qualification of AI tools, the draft guidance includes how bias and representativeness can be considered as part of credibility assessment for a model in a defined context of use and activities for risk mitigation the developer can undertake to further enhance the credibility of a tool.**

Finally, in order to avoid the adoption of disjointed frameworks for regulatory oversight that will make it difficult for AI developers to manage compliance with quality and privacy controls, **PMC recommends**

that oversight should be appropriate to the technology and harmonized with other regulatory frameworks AI may be subject to, including both domestic and global regulatory frameworks. Through participation in venues such as the International Council for Harmonization and International Medical Device Regulators Forum, FDA can ensure that harmonization benefits innovation and broader adoption of AI by avoiding duplicative, overlapping, and conflicting jurisdiction of regulatory authorities.

Conclusion

PMC appreciates FDA's interest in advancing in the use of AI to support regulatory decision making for drugs and biologics. We look forward to working with you and your colleagues to finalize this guidance so that it considers the current and future role of AI in advancing personalized medicine. If you have any questions about the content of this letter, please contact me at cbens@personalizedmedicinecoalition.org, or David Davenport, PMC's Director of Public and Science Policy, at ddavenport@personalizedmedicinecoalition.org.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

[i] U.S. Food and Drug Administration. *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision Making for Drug and Biological Products: Draft Guidance for Industry and Other Interested Parties.* January 2025. *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-artificial-intelligence-support-regulatory-decision-making-drug-and-biological* (Accessed April 1, 2025).

[ii] C.S. Ajmal, S. Yerram, V. Abishek, et al. "Innovative Approaches in Regulatory Affairs: Leveraging Artificial Intelligence and Machine Learning for Efficient Compliance and Decision-Making." *AAPS Journal* 27 (2025): 22. https://doi.org/10.1208/s12248-024-01006-5 (Accessed April 1, 2025).