ConnectedHealthInitiative

April 7, 2025

Commissioner Martin Makary
U.S. Food & Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Silver Spring, Maryland 20993-0002

RE: ***Connected Health Initiative Comments on the Food and Drug Administration's Draft Guidance for Industry and Other Interested Parties, Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products [Docket No. FDA-2024-D-4689; 90 FR 1157]***

Dear Commissioner Makary:

The Connected Health Initiative (CHI) writes to provide input on the Food and Drug Administration's (FDA) draft guidance for industry entitled "Considerations for the Use of Artificial Intelligence To Support Regulatory Decision-Making for Drug and Biological Products."[1] CHI is the leading effort by stakeholders across the connected health ecosystem to responsibly encourage the use of digital health innovations and support an environment in which patients and consumers can see improvements in their health. We seek essential policy changes that will help all Americans benefit from an information and communications technology-enabled American healthcare system. For more information, see www.connectedhi.com.

CHI is a longtime active advocate for the increased use of new and innovative digital technologies in both the prevention and treatment of disease and we appreciate the FDA's consistent collaboration on digital health-related technologies to responsibly streamline their pathway to the market. AI-enabled software functions are radically improving the American healthcare system, including clinical outcomes, and will continue to do so. Mobile app-enabled telehealth and remote monitoring of patient-generated health data continues to represent the most promising avenue for improved care quality, reduced hospitalizations, avoidance of complications, and improved satisfaction, particularly for the chronically ill.

AI is an evolving constellation of technologies that enable computers to simulate elements of human thinking, such as learning and reasoning. An encompassing term, AI entails a range of approaches and technologies, such as machine learning (ML), where algorithms use data, learn from it, and apply their newly-learned lessons to make informed decisions, and deep learning, where an algorithm based on the way neurons and synapses in the brain change as they are

[1] 90 FR 1157.

exposed to new inputs allows for independent or assisted decision-making. Already, AI-driven algorithmic decision tools and predictive analytics have substantial direct and indirect effects in consumer and enterprise contexts and show no signs of slowing in the future. Across use cases and sectors, AI has incredible potential to improve consumers' lives through faster and better-informed decision-making, enabled by cutting-edge distributed cloud computing, with drug and biologic product development being no exception. As AI systems, powered by streams of data and advanced algorithms, continue to improve services and generate new business models, the fundamental transformation of economies across the globe will only accelerate. Nonetheless, AI also has the potential to raise a variety of unique considerations for policymakers.

Initially, CHI supports the Center for Drug Evaluation and Research's (CDER) coordination with FDA's Center for Devices and Radiological Health (CDRH), Center for Biologics Evaluation and Research (CBER), Center for Veterinary Medicine (CVM), the Oncology Center of Excellence (OCE), the Office of Combination Products (OCP), and the Office of Inspections and Investigations (OII). Because CDRH oversees market entry for AI-based software as a medical device (SaMD) across a wide range of conditions and provides iterative and leading guidance on AI and ML (e.g., the avoidance of automation bias in the context of clinical decision support[2]), we encourage full alignment with its approach across all relevant Centers and Offices. CDRH's Digital Health Center of Excellence continues to leverage total product lifecycle oversight to further the potential that AI has to deliver safe and effective software functionality that improves patients' quality of care.[3] Even more recently, FDA has proposed new guidance addressing what information should be included in a Predetermined Change Control Plan that may be provided in a marketing submission for machine learning-enabled device software functions,[4] on which CHI has provided supportive comments.[5] Misalignment or divergence from with CDRH's approach to AI would lend to confusion and conflicting approaches within the health AI space, and the CHI urges for revisions to CDER's Discussion Paper to align with CDRH's risk-based approach to AI.

CHI believes that the FDA's proposed guidance would generally advance an approach to regulating AI in medical products emphasizes several key principles to ensure safety, effectiveness, and innovation. Because AI applications in medical products vary significantly in their scope and associated risks, FDA primarily evaluates risk based on two factors: the influence of the AI model and the consequences of decisions made using that model. Risk-based oversight is already integral to FDA's regulation of medical products, and extending this principle to AI would allow developers and sponsors to implement tailored risk mitigations specific to their use cases rather than relying on a one-size-fits-all approach.

CHI also supports FDA's embracing a total product lifecycle perspective, which spans from ideation and development to real-world implementation and ongoing monitoring. This approach aligns with international standards, such as ISO 42001, which provides guidelines for managing AI systems within organizations. By adopting lifecycle management strategies, the FDA promotes

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[2] https://www.fda.gov/media/109618/download.

[3] https://www.fda.gov/media/122535/download; https://www.fda.gov/news-events/press-announcements/fda-releases-artificial-intelligencemachine-learning-action-plan.

[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/marketing-submission-recommendations-predetermined-change-control-plan-artificial.

[5] https://www.regulations.gov/comment/FDA-2022-D-2628-0032.

continuous oversight of AI systems to ensure they remain reliable and compliant as technologies evolve.

We note that, while FDA's guidance emphasizes transparency in training and development data, this focus may be excessive. While knowing the data used to train a model is important, it does not guarantee performance in specific real-world applications. Instead, the agency should prioritize testing AI models in their intended settings with relevant populations. Transparency should center on performance results rather than solely on development data. Proprietary information, such as training datasets or their sources, may not always be accessible—especially when medical product sponsors use third-party AI models hosted by cloud service providers. To address this challenge, the FDA could assess existing documentation provided by developers regarding AI system capabilities, limitations, intended use guidelines, and performance outcomes.

CHI also urges FDA's involved Centers and Offices to appropriately frame its discussion of emerging technologies and how their responsible deployment can improve and streamline processes. We note that CDER's discussion paper preceding this draft guidance stated that "existing quality agreements between the manufacturer and a third party (e.g., for cloud data management) may have gaps with respect to managing the risks of AI in the context of manufacturing monitoring and control[,]…lead[ing] to challenges [during inspections] in ensuring that the third-party creates and updates AI software with appropriate safeguards for data safety and security" and that "the ongoing interactions between cloud applications and process controls could complicate the ability to establish data traceability, create potential cybersecurity vulnerabilities, and require evaluation of the procedures in place to monitor data integrity vulnerabilities during an inspection."[6] Neither of these speculative assertions are supported by evidence, nor do they align with the experiences of the healthcare sector. While these assertions do not appear in FDA's draft guidance on AI and ML's use in the development of drug and biological products, we strongly encourage FDA to ensure that its policies reflect that cloud computing enables secure, ubiquitous, convenient, on-demand network access to a shared pool of configurable computing resources (e.g., networks, servers, storage, applications, and services) that can be rapidly provisioned and released with minimal management effort or service provider interaction. Cloud computing allows organizations to leverage servers and access computer system resources—such as computing power, storage, and network power—to meet their changing technology needs and are increasingly relied upon throughout the healthcare ecosystem. The capabilities of cloud computing are necessary tools for advancing FDA's interests and goals in pharmaceutical manufacturing data and recordkeeping.

Building on the above, CHI urges FDA's guidance to align with the following consensus recommendations from the digital health community for policymakers seeking to address the role of AI in healthcare:

1. **Research:** FDA should support and facilitate research and development of AI by prioritizing and providing sufficient funding while also ensuring adequate incentives (e.g., streamlined availability of data to developers) are in place to encourage private and non-profit sector research. Transparency research should be a priority and involve collaboration among all

[6] FDA, *Using Artificial Intelligence & Machine Learning in the Development of Drug & Biological Products, Discussion Paper and Request for Feedback* at 6-7, available at https://www.fda.gov/media/167973/download.

affected stakeholders who must responsibly address the ethical, social, economic, and legal implications that may result from AI applications.

2. **Quality Assurance and Oversight**: FDA should utilize risk-based approaches to ensure that the use of AI aligns with the recognized standards of safety and efficacy. Providers, technology developers and vendors, and other stakeholders all benefit from understanding the distribution of risk and liability in building, testing, and using AI tools. Policy frameworks addressing liability should ensure the appropriate distribution and mitigation of risk and liability. Specifically, those in the value chain with the ability to minimize risks based on their knowledge and ability to mitigate should have appropriate incentives to do so. Some recommended guidelines include:
    - Ensuring AI is safe and efficacious.
    - Supporting that algorithms, datasets, and decisions are appropriately auditable.
    - Encouraging AI developers to consistently utilize rigorous quality assurance procedures and enabling them to document their methods and results.
    - Requiring those developing, offering, or testing AI systems to provide truthful and easy to understand representations regarding intended use and risks that would be reasonably understood by those intended, as well as expected, to use the AI solution.
    - Ensuring that adverse events are timely reported to relevant oversight bodies for appropriate investigation and corrective action.

3. **Thoughtful Design:** FDA should require design of AI systems that are informed by real-world workflows, human-centered design and usability principles, and end-user needs. AI systems solutions should facilitate a transition to changes in the delivery of goods and services that benefit consumers and businesses. The design, development, and success of AI should leverage collaboration and dialogue among users, AI technology developers, and other stakeholders in order to have all perspectives reflected in AI solutions.

4. **Access and Affordability:** FDA should ensure AI systems are accessible and affordable. Significant resources may be required to scale systems. Policymakers should take steps to remedy the uneven distribution of resources and access and put policies in place that incent investment in building infrastructure, preparing personnel and training, as well as developing, validating, and maintaining AI systems with an eye toward ensuring value.

5. **Ethics:** The success of AI depends on ethical use. FDA policies will need to promote many of the existing and emerging ethical norms for broader adherence by AI technologists, innovators, computer scientists, and those who use such systems. FDA should:
    - Ensure that AI solutions align with all relevant ethical obligations, from design to development to use.
    - Encourage the development of new ethical guidelines to address emerging issues with the use of AI, as needed.
    - Maintain consistency with international conventions on human rights.
    - Ensure that AI is inclusive such that AI solutions beneficial to consumers are developed across socioeconomic, age, gender, geographic origin, and other groupings.

- Reflect that AI tools may reveal extremely sensitive and private information about a user and ensure that laws protect such information from being used to discriminate against certain consumers.

6. **Modernized Privacy and Security Frameworks:** While the types of data items analyzed by AI and other technologies are not new, this analysis will provide greater potential utility of those data items to other individuals, entities, and machines. Thus, there are many new uses for, and ways to analyze, the collected data. This raises privacy issues and questions surrounding consent to use data in a particular way (e.g., research, commercial product/service development). It also offers the potential for more powerful and granular access controls for consumers. Accordingly, any policy framework should address the topics of privacy, consent, and modern technological capabilities as a part of the policy development process. Policy frameworks must be coordinated and scalable while assuring that an individual's data is properly protected, while also allowing the flow of information and responsible evolution of AI. This information is necessary to provide and promote high-quality AI applications. Finally, with proper protections in place, policy frameworks should also promote data access, including open access to appropriate machine-readable public data, development of a culture of securely sharing data with external partners, and explicit communication of allowable use with periodic review of informed consent.

7. **Collaboration and Interoperability:** FDA should enable eased data access and use through creating a culture of cooperation, trust, and openness among policymakers, AI technology developers and users, and the public.

8. **Bias:** The bias inherent in all data, as well as errors, will remain one of the more pressing issues with AI systems that utilize machine learning techniques in particular. Any regulatory action should address data provenance and bias issues present in the development and uses of AI solutions. FDA should:
    - Require the identification, disclosure, and mitigation of bias while encouraging access to databases.
    - Ensure that data bias does not cause harm to users or consumers.

9. **Education:** FDA should support education for the advancement of AI, promote examples that demonstrate the success of AI, and encourage stakeholder engagements to keep frameworks responsive to emerging opportunities and challenges.
    - Consumers should be educated as to the use of AI in the service they are using.
    - Academic education should include curriculum that will advance the understanding of and ability to use AI solutions.

10. **Intellectual Property:** The protection of IP rights is critical to the evolution of AI. In developing approaches and frameworks for AI governance, policymakers should be mindful of how current legal protections apply in circumstances involving AI and ensure that compliance measures and requirements do not undercut IP or trade secrets.

CHI has also developed the following resources, which we urge FDA to align its approach to AI with:

- CHI's *Health AI Policy Principles*, a comprehensive set of recommendations on the areas that should be addressed by policymakers examining AI's use in healthcare, and how they

should be addressed (https://connectedhi.com/wp-content/uploads/2022/02/Policy-Principles-for-AI.pdf)

- CHI's *Health AI Good Machine Learning Practices*, a recommended pathway for the FDA to ensure innovation in machine learning-enabled medical devices, including for continuously learning algorithms, while protecting patient safety: https://connectedhi.com/wp-content/uploads/2022/04/CHIAITaskForceGMLPs.pdf
- CHI's *Advancing Transparency for Artificial Intelligence in the Healthcare Ecosystem*, a proposal on ways to increase the transparency of and trust in health AI tools, particularly for care teams and patients (https://connectedhi.com/wp-content/uploads/2022/02/AdvancingTransparencyforArtificialIntelligenceintheHealthcareEcosystem.pdf)
- CHI's *Health AI Roles & Interdependency Framework*, which proposes clear definitions of stakeholders across the healthcare AI value chain, from development to distribution, deployment, and end use; and suggests roles for supporting safety, ethical use, and fairness for each of these important stakeholder groups that are intended to illuminate the interdependencies between these actors, thus advancing the shared responsibility concept (https://connectedhi.com/wp-content/uploads/2024/02/CHI-Health-AI-Roles.pdf)
- CHI's issue paper on the impact of standard-essential patent licensing abuses on digital healthcare (https://connectedhi.com/wp-content/uploads/2025/03/CHI-Issue-Paper-Healthcare-and-Standard-Essential-Patents-Feb-202568.pdf)

CHI appreciates the opportunity to submit its comments to the FDA and urges its thoughtful consideration of the above input.

Sincerely,

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