Via Electronic Submission to: www.regulations.gov

July 3, 2023

Dockets Management Staff
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Docket No. FDA-2022-D-2628: Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML) – Enabled Device Software Functions; Draft Guidance for Industry and Food and Drug Administration Staff

To Whom it May Concern:

On behalf of its membership, the Pharmacy Health Information Technology Collaborative (PHIT) is pleased to submit comments for *Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML) – Enabled Device Software Functions; Draft Guidance for Industry and Food and Drug Administration Staff.* PHIT has been involved with the federal agencies, including the Department of Health and Human Services (HHS) Office of the National Coordinator (ONC), the Food and Drug Administration (FDA), and the Centers for Medicare & Medicaid Services (CMS), in developing the national health information technology (HIT) framework for implementing secure access of electronic health information to improve health outcomes since 2010.

Pharmacists provide essential, patient-centered care services to their patients. Pharmacists use health IT, medical devices, provider directories, telehealth, e-prescribing (eRx), electronic medical record (EMR)/electronic health record (EHR) systems, and certified EHR technology (CEHRT) to help manage patients' health needs. PHIT supports the use of these systems, which are important to pharmacists in working with other health care providers to provide longitudinal person-centered care planning, needed medications, and transmit patient information related to overall patient care, transitions of care, immunization, medication lists, medication allergies, allergy reactions, patient problem lists, smoking status, and social determinants of health (SDOH). Pharmacists also use health IT for reporting to public health agencies (e.g., immunization reporting), clinical decision support services/knowledge artifacts, drug formulary checking, and comprehensive medication management (CMM).

General Comment

PHIT appreciates the direction of the draft guidance and, in principle, agrees with the guidance and supports the recommendations made by the Food and Drug Administration to assure that new versions released have the changes in the predetermined control plan.

Specific Comments

V. Policy for Predetermined Change Control Plans

PHIT supports the proposed policy that modifications made to machine learning-enabled device function (ML-DSF) that are not specified or implemented in accordance with the Predetermined Chance Control Plan (PCCP) would require a new marketing submission, and if continued distribution of the ML-DSF without submitting a new marketing submission would constitute adulteration/misbranding under the Food Drug & Cosmetic Act.

V(C). Identifying PCCP in a Marketing Submission

PHIT agrees that for ML-DSFs with an authorized PCCP, the labeling should explain that the device incorporates machine learning and has a PCCP so that users are aware that the device may require users to perform software updates and that such updates may modify the device's performance, inputs, or use.

VI(C). Types of Modifications

The modifications outlined that may be acceptable with a PCCP are the most important part of the draft guidance for PHIT and pharmacists. The types of acceptable modifications include those modifications related to quantitative measures of ML-DSF performance specifications, device inputs to the ML-DSF, and limited modifications related to the device's use and performance.

VII(B)(1). Content of the Modification Protocol Section: Data Management Practices

Critical to data management practices, particularly regarding ML-DSF training, is to ensure that algorithms are taken into consideration and that clinicians (e.g., pharmacists) can change and affect algorithms if there are issues. Because ML is new and could have patient efficacy issues, clinicians need to intervene if there is problem, especially if potential algorithmic and predictive model biases are detected for a patient population.

The Office of the National Coordinator for Health Information Technology is also looking at artificial intelligence, algorithms, and predictive models in health care in its recently proposed rule for *Health Data, Technology, and Interoperability: Certification Program Updates, Algorithm Transparency, and Information Sharing Rule*. PHIT wrote in its June 20 comments to ONC that clinician trust in artificial intelligence (AI) and machine learning (ML)-based predictive decision support interventions (DSIs) will be crucial for adoption. PHIT believes that advances in predictive modeling based on AL/ML have the potential for improving clinical care, including

pharmacist provided person-centered care, and patient outcomes provided predictive DSI is unbiased; trustworthy; fair, appropriate, valid, effective, and safe (FAVES) when applied to medications; and the information from these models is presented in an effective manner for sound decision making.

To ensure that predictive DSI is not biased, developers of AI/ML and certified health IT with health IT modules need to address issues, such as health equity, information privacy and security, patient safety, and data stewardship, including data de-identification, to prevent algorithmic bias. Algorithmic bias, which is not new, can exacerbate social inequities in health care.[1] Although a number of intervention risk management requirements for predictive DSI are proposed in this rulemaking, including submitting "real world testing plans and results," the ONC proposal does not appear to address or require equity in testing in these plans for AL/ML across patient population to limit potential biases, particularly those biases pertaining to race and ethnicity, which are directly related to health care inequities and SDOH.

"AI utilizes algorithms to assess data from the world, make representation of that data, and use that information to make an inference."[2] Among the worldwide data accessed is health care data, which may not necessarily be an equitable and accurate representation of certain patient populations in the United States. These algorithms that use evidence-based data for medications, clinical trials, may be the basis for population bias. In their 2019 paper, "Artificial intelligence and algorithmic bias: implications for health systems," Panch, Mattie, and Atun define "algorithmic bias in the context of AI and health systems as: 'the instances when the application of an algorithm that compounds existing inequities in socioeconomic status, race, ethnic background, religion, gender, disability, or sexual orientation to amply them and adversely impact inequities in health systems.'"[3]

Health care and health care systems will face challenges in addressing algorithmic biases especially as it relates to medications. Federal guidance, requirements, and harmonization are needed to address this. PHIT also believes there will likely be additional need for those who are users AI/ML-DSF and how those users should interact with the manufacturer. FDA should look further at this and address it either in this proposed draft guidance or in separate rulemaking. The proposed draft guidance could be a first step.

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The Pharmacy HIT Collaborative comprises the major national pharmacy associations, representing 250,000 members, including those in pharmacy education and accreditation. PHIT's membership is composed of the key national pharmacy associations involved in health IT, the National Council for Prescription Drug Programs, and 13 associate members encompassing e-prescribing, health information networks, transaction processing networks, pharmacy companies, system vendors, pharmaceutical manufacturers, and other organizations that support pharmacists' services.

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[1] Katherine J. Igoe, "Algorithmic Bias in Health Care Exacerbates Social Inequities – How to Prevent It," Harvard T.H. Chan School of Public Health, March 12, 2021. https://www.hsph.harvard.edu/ecpe/how-to-prevent-algorithmic-bias-in-health-care/

[2] Ibid.

[3] Trishan Panch, Heather Mattie, and Rifat Atun, "Artificial intelligence and algorithmic bias: implications for health systems," Journal of Global Health, December 9, 2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6875681/

As the leading authority in pharmacy health information technology, PHIT's vision and mission are to ensure the U.S. health IT infrastructure better enables pharmacists to optimize person-centered care. Supporting and advancing the use, usability, and interoperability of health IT by pharmacists for person-centered care, PHIT identifies and voices the health IT needs of pharmacists; promotes awareness of functionality and pharmacists' use of health IT; provides resources, guidance, and support for the adoption and implementation of standards-driven health IT; and guides health IT standards development to address pharmacists' needs. For additional information, visit www.pharmacyhit.org.

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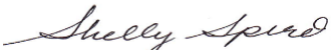
On behalf of PHIT, thank you again for the opportunity to comment on *Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML) – Enabled Device Software Functions; Draft Guidance for Industry and Food and Drug Administration Staff*.

For more information, contact Shelly Spiro, executive director, Pharmacy HIT Collaborative, at shelly@pharmacyhit.org.

Respectfully submitted,



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