February 6, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: *Comments of the Connected Health Initiative regarding the Food and Drug Administration's Draft Guidance for Industry and Food and Drug Administration Staff on Clinical and Patient Decision Support Software (Docket No. FDA-2017-D-6569)*

ACT | The App Association's Connected Health Initiative (CHI)[1] writes to provide input to the Food and Drug Administration (FDA) on its draft guidance on the scope of its regulatory oversight of clinical decision support (CDS) software intended for healthcare professionals and patient decision support (PDS) software intended for patients and caregivers who are not healthcare professionals.[2] CHI and its members appreciate the FDA's progress in moving to provide much-needed clarity in the regulation of CDS. Healthcare companies and innovators depend on transparent legal and regulatory responsibilities to help Americans fully realize the potential of mobile health apps. CHI applauds the FDA for its leadership in drafting guidance on CDS and PDS software and appreciates this opportunity to provide input.

CHI is the leading effort by stakeholders across the connected health ecosystem to clarify outdated health regulations, encourage the use of remote patient monitoring (RPM), and support an environment in which patients and consumers can see improvement in their health. We seek partnerships and activities that realize the benefits of an information and communications technology-enabled American healthcare system. CHI members and stakeholders actively participate in the administration of healthcare through connected technologies and medical devices. We strongly believe that by streamlining regulatory processes and providing a clear approach to connected health hardware and software technologies, the FDA can play a central role in creating a cost-effective, patient-centered, and quality-driven healthcare system for all Americans.

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[1] http://www.connectedhi.com/

[2] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM587819.pdf

CHI appreciates the FDA's continued examination of the changing, and increasingly important, role of software in medical devices.[3] CDS software applications can vastly improve patient care by providing caregivers with data and trends from countless patient treatments and outcomes to better inform their medical decisions. In the past, caregivers could only rely on their personal experiences, education, and research, but with the assistance of CDS software, health systems of all sizes can improve and harmonize their caregivers' efficiency and patient outcomes, particularly in the treatment of complex chronic conditions. Chronic conditions would benefit from large amounts of data being collected and analyzed through precision medicine initiatives (e.g., automating literature reviews to gain knowledge about cutting-edge treatments based on the patient's demographics, health history, and test results).

Despite the incredible potential CDS software offers to American caregivers and patients, these solutions are grossly underutilized today. Without FDA's regulatory clarity around the use of CDS software, mobile devices, and apps, these solutions are unlikely to be leveraged to their full potential.

The FDA's efforts pursuant to the 21st Century Cures (21CC) Act are an example of the agency's willingness to embrace advanced technology and connectivity in the healthcare continuum. Not only does this FDA guidance satisfy the rules within the 21st Century Cures Act, but it is also good public policy and is consistent with Congressional goals in the Food and Drug Administration Safety and Innovation Act of 2012 to promote innovation, protect patient safety, and avoid regulatory duplication.

CHI applauds the FDA for putting forward its draft guidance on CDS software and commits to partner with the FDA to make it as impactful as possible. We will also help the FDA modernize its regulation of medical devices to promote investment and innovation in the software and hardware used to improve American patient outcomes. We generally support the FDA's movement to develop this much-needed guidance, which will clarify the CDS software exempt from FDA regulation and show how CDS software subject to FDA regulation may be treated under the FDA's scalable risk-based approach.

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[3] E.g., [cite to FDA pre-cert program]

Building on the above, CHI offers the following specific comments on the FDA's draft CDS software guidance:

- ***Provide clarity in the FDA's definition of CDS software*** – The FDA proposes to define CDS software by referring to the first, second, and third criteria of section 520(o)(1)(E), which represents the list of CDS software Congress has mandated to be exempted from FDA regulation. CHI strongly recommends that the FDA provide a clear definition of what CDS software is, in line with the criteria of section 520(o)(1)(E) as well as government and industry consensus on CDS software.[4]

- ***Provide clarity regarding the meaning of "a pattern or signal from a signal acquisition system"*** – Using guidance based on Section 520(o)(1)(E), the FDA proposes that CDS software intended to "acquire, process, or analyze a medical image, a signal from an in vitro diagnostic device, or a pattern or signal from a signal acquisition system" will still be considered a medical device. The FDA also proposes to define a "signal acquisition system" as "the electronic circuitry and control processor that receives, as inputs, signals from sensors that are within, attached to (e.g., EEG, ECG), or external to (e.g., CT, MRI) the human body or sample from the human body (e.g., digital pathology)." However, the FDA's examples do not present a clear picture of what is, and is not, a "pattern or signal from a signal acquisition system." Amongst the examples, sources of data are raised in both the device and non-device context that meet the FDA's proposed definition.

  Unclear examples include "software that analyzes multiple physiological signals (e.g., sweat, heart rate, eye movement, breathing) to monitor whether a person is having a heart attack or narcolepsy episode," "ST-segment measurements from ECG signals," "a report based on arterial blood gas results," and others. Without clarity in the text or the examples within the guidance, developers may be forced to conclude that all their CDS software, with a few clear exceptions, utilizes physiologic data attained through a signal acquisition system.

- ***Provide clarity regarding the definition of a "physiological signals"*** – CHI is concerned that the FDA's proposed definition of "physiological signals" is overbroad and would effectively capture all CDS software, including software that utilizes physiologic data attained through an intermediary that analyzed the data, like an electronic health record. CHI believes that unless altered, the FDA's approach would classify the vast majority of innovative CDS software functions as medical devices subject to FDA oversight, including those that pose a low risk to patients.

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[4] E.g., https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/Downloads/ClinicalDecisionSupport_Tipsheet-.pdf; Health IT, *Clinical Decision Support (CDS)*, http://www.healthit.gov/policy-researchers-implementers/clinical-decision-support-cds

- o We do not believe that such a sweeping approach to physiological signals, which would include technologies and devices like consumer wearables and electronic health records, aligns with the intent of Congress under the 21CC Act. We urge the FDA to add the following underlined text to Line 177: "Products that directly acquire an image or physiological signal…"; and for the addition of the following underlined text in Footnote 2: "A signal acquisition system is the electronic circuitry and control processor that directly receives…"

- *Provide clarity regarding "independent review"* – The FDA proposes that under Section 520(o)(1)(E)(iii), "the CDS function must be intended to enable health care professionals to independently review the basis for the recommendations presented by the software so that they do not rely primarily on such recommendations, but rather on their own judgment, to make clinical decisions for individual patient." The FDA also states that "[a] practitioner would be unable to independently evaluate the basis of a recommendation if the recommendation were based on non-public information or information whose meaning could not be expected to be independently understood by the intended health care professional user."

  - o The FDA states that published literature and clinical practice guidelines are acceptable public information. However, the FDA should include other key sources of information to ensure the independent review is not too narrowly scoped. For example, for-profit and non-profit entities release white papers and other articles that offer the ability to conduct an independent review. CHI requests that the FDA clearly indicate that sources' previously published literature and clinical practice guidelines be allowed in independent reviews. FDA is encouraged to include "reasonably available sources" or similar phrasing.

- Additionally, some particularly innovative areas of health care delivery do not have generally accepted or publicly available guidelines to form the basis of the CDS or PDS recommendations. Some generally accepted, consensus-based guidelines or standards can be limiting and may not make sense in every clinical context. For example, with the use of patient-generated health data, the PROMIS measures are the typical "standard" within the community—but those measures contemplate only one-way flow of information, i.e. survey data. Technology can enable much more than that, including the bi-directional, engaging "conversational" flow of data that is described in this hypothetical scenario, and the FDA is encouraged to account for this gap in its CDS guidance.

  - As an example of software that will require continued regulatory oversight, CDS software that utilizes a "proprietary algorithm" to recommend a specific treatment would be considered a medical device and subject to regulatory oversight. Countless CDS software innovations are, and will be, built upon proprietary algorithms. The fact that an algorithm is proprietary does not mean the CDS software's recommendation cannot be "identified and easily accessible to the intended user, understandable by the intended user…, and publicly available." There are many reasons why an algorithm would not be disclosed, but could be adequately described. The algorithm/decision tree/rationale provided by CDS software may well be in use before the software is created, and the software's processes and results may further be published in literature that is publicly available. Proprietary algorithms may be "easily accessible" to, "understandable," and "well-understood" by health care providers as well as the general public through explaining logic paths. Rule-based algorithms that can be pre-validated by healthcare providers using public clinical guidelines should enjoy enforcement discretion, including algorithms that use machine learning within the algorithm to predictably tailor the analysis.

    - An algorithm's proprietary nature does not always correlate with the ability to review the basis for its recommendations (e.g., a simple licensing agreement can provide access to a healthcare provider for the purposes of independent verification). CHI requests that the FDA delete the word "proprietary" from Line 329.

    - With the above changes, we request that the FDA provide at least one example of a CDS software algorithm that is exempt from regulation and an example of a CDS software algorithm that is not exempt from regulation.

- ***Squarely address artificial intelligence and machine learning*** –Artificial intelligence (AI) and machine learning have incredible potential to improve treatments and patient outcomes, including through CDS software. CHI urges the FDA to directly address the role of AI and machine learning in its CDS software guidance. Innovative CDS software will likely utilize AI and machine learning to improve the software's processes, and these innovations should enjoy regulatory exemption or relief consistent with Congressional intent to reduce barriers to

innovation in CDS software. As long as the CDS software's processes are transparent and can be examined to ensure clinicians could independently reach the same recommendation, CDS software should satisfy the FDA's four-pronged test and be exempt from FDA regulatory oversight. If the AI or machine learning processes are primarily relied upon by a healthcare provider and cannot be independently verified, CHI believes the CDS software would be subject to FDA oversight as a medical device. The connected health industry, and software developers in particular, will benefit from the FDA directly addressing AI and machine learning in this guidance – even if the FDA merely indicates that it intends to address AI and machine learning in future, standalone guidance.

- ***Additional rationale for each example in the guidance*** – We believe stakeholders would benefit immensely if the FDA included rationale as to why each example is considered a medical device.

- ***Changes to proposed examples and new examples to include in the guidance*** – We propose that the FDA incorporate the following changes and additions into the examples provided within the guidance:

  o CHI urges FDA to add "or machine learning" after the phrase "rule-based tools" on Line 259 of the draft guidance, consistent with our comment provided above.

  o Consistent with the four-factor test established in section 520(o)(1)(E), CHI recommends adding the following examples to the category of CDS software that is exempt from FDA regulation:

    ▪ "A software function that generates potential healthcare approaches that are specific to the patient by matching patient data with reasonably available sources, with the aim of helping the caregiver make a diagnosis or treatment decision. Such software leaves the diagnosis or treatment decision solely to the judgement of the healthcare professional."

    ▪ "A software function that utilizes rule-based tools or machine learning to measure patient-specific data points based on parameters set by the healthcare provider, alerts the healthcare provider and/or patient when data points exceed healthcare provider-set thresholds, and is not primarily relied upon by the healthcare provider in making an independent diagnosis or treatment decisions."

  o CHI recommends the following change to the proposed example in lines 325-328 to replace "algorithm undisclosed to the user" with "algorithm-based approach that is primarily relied upon by the healthcare provider and is not independently verifiable."

  o CHI recommends the following change to the proposed example in lines 329-331 to replace "proprietary algorithm" with "algorithm primarily relied upon by the healthcare provider."

- ***Support the inclusion of Patient Decision Support (PDS) software within CDS software guidance; request additional clarity regarding "healthcare provider oversight"*** – CHI appreciates that the FDA addresses PDS in the Draft Guidance. We also support the FDA's proposal to use an approach similar to CDS for PDS software, which includes messaging specific to PDS software. However, we urge the FDA to provide a flexible and realistic approach to enabling independent verification by a patient or non-healthcare provider, consistent with the above discussion on independent verification for CDS software. We urge the FDA to ensure its approach to PDS software aligns with the treatment of CDS software, as practically as possible.

  - CHI requests additional clarity to a statement made by the FDA that PDS software includes software that "does not recommend changes in dose or drug discontinuation that healthcare providers do not oversee (unless drug labeling includes such recommendations)." We interpret this statement to mean the healthcare provider has instructed the patient on how to use the PDS software, not that such a communication must occur every time the patient uses the PDS software. The latter would be an unworkable scenario and create unnecessary burdens for the healthcare provider.

- ***Support for Center for Devices and Radiological Health (CDRH) collaboration with the Center for Drug Evaluation and Research (CDER)*** – CHI applauds the CDRH for working with CDER in the development of the Draft Guidance. The combination of digital health and pharmaceutical perspectives provides immense benefits to countless American patients. CHI supports the FDA's proposal to ensure FDA-compliant recommendations on the use of a prescription drug is not considered a medical device.

We appreciate the opportunity to provide input on the FDA's Draft Guidance and request that our views be considered as the FDA finalizes its CDS and PDS software guidance. We are available to further discuss our views with the FDA.

Sincerely,

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