ConnectedHealth

December 26, 2019

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RE: *Comments of the Connected Health Initiative Regarding the Food and Drug Administration's* Draft Guidance for Industry and Food and Drug Administration Staff on Clinical and Patient Decision Support Software *(Docket No. FDA-2017-D-6569)*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Connected Health Initiative (CHI)[1] writes to provide input to the Food and Drug Administration (FDA) on its draft guidance regarding the scope of its regulatory oversight of clinical decision support (CDS) software intended for healthcare professionals and patient decision support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 FDA's progress in moving to provide much-needed clarity on the regulation of CDS. Healthcare companies and innovators depend on transparent legal and regulatory responsibilities to fully realize the potential of mobile health apps. CHI thanks 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CHI is the leading effort by stakeholders across the connected health ecosystem to clarify outdated health regulations, encourage the use of remote patient monitoring (RPM), and support an environment in which patients and consumers can see improvement in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 out partnerships and opportunities 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 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. Specifically, CDS software can be impactful in the treatment of complex chronic conditions. Chronic condition research and treatment would benefit from large amounts of data 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 meet their full potential.

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. FDA's guidance must satisfy the rules within the 21st Century Cures Act, and serve as good public policy 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.

We generally support FDA's movement to develop this guidance, which will clarify the CDS software exempt from FDA regulation and show how CDS software subject to FDA regulation may be treated under FDA's scalable risk-based approach.

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

- ***Directly addressing how new CDS software guidance impacts regulatory responsibilities.*** CHI requests that, as appropriate throughout the new CDS software guidance, FDA address how its new guidance will address the regulatory responsibilities of stakeholders. For example, it would be helpful for FDA to discuss how the norms for addressing product changes are impacted by its CDS software guidance.
- ***Provide clarity in FDA's definition of CDS software.*** The FDA has proposed a CDS definition that is expansive. For example, the information in the guidance that would be used by a stakeholder to determine whether their device faces FDA regulation rests across different sections and tables in the Draft Guidance. This approach makes it difficult to apply FDA's guidance to software functions in

[3] E.g., https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program.

order to determine whether FDA regulation applies to the specific software function. To provide clarity for stakeholders, we recommend that FDA raise the profile of Table 3 ("Summary of Regulatory Policy for CDS Software Functions") in the Draft Guidance, including creating a decision flowchart for stakeholders seeking to evaluate a software function that includes references to Table 3 and other key guidance in the document as well as key FDA resources located outside of the CDS guidance. CHI strongly recommends that 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]

- CHI believes that the term "medical image" should have a scope that includes images collected by medical devices, and not images collected by non-medical devices/software functions (and not limited to radiology images). Should the image be transferred to a medical device and is used for a medical purpose, the originator of the image would not become a medical device.
- Regarding the meaning of "a pattern or signal from a signal acquisition system":
  - In providing further clarity as to the meaning of "physiologic signals," FDA should help define the term "physiologic" broadly to include characteristics of human functioning and well-being for the prevention or treatment of disease. Recognizing that this definition will have a wide impact on digital health past the FDA's approach to CDS software, including in the context of Medicare reimbursement where the Centers for Medicare and Medicaid Services have provided new payments for eligible practioner time spent evaluating patient generated health data (PGHD) collected through "remote physiologic monitoring" through medical devices as defined by FDA.
  - Further, for purposes of FDA's approach to CDS, we urge FDA to ensure alignment with Section 520(o)(1)(E) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) by appropriately defining "signal" to be the immediate output of an algorithm evaluating device measurements. FDA should not consider the raw measurements themselves to be "signals" for the purposes of CDS regulation/non-regulation.
  - FDA should refine the scope of "signal acquisition system" to include systems that are medical devices, and not non-medical devices/software functions. Should a signal be transferred to a

[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

medical device and is used for a medical purpose, the originator of the signal would not become a medical device.

- FDA should provide further clarity on how electronic health record platforms fit into FDA's new approach to CDS software. While electronic patient record software is excluded from the medical device definition in 21CC, it is unclear as to how the FDA may approach complex scenarios where regulated medical data may be provided to non-device CDS software.
- Regarding the exclusion criteria addressing independent review, FDA proposes that the CDS function must be intended to enable healthcare 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 each individual patient. FDA also states that a practitioner should 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 healthcare professional user. CHI supports that Software as a Medical Device (SaMD) developers should 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 solution.
    - FDA should include the key sources of information available for independent review. For example, for-profit and non-profit entities release white papers and data that offer the ability to conduct an independent review. CHI requests that FDA clearly indicate that sources' previously published literature and clinical practice guidelines be allowed in independent reviews, along with other relevant information to independent review. The CHI encourages the FDA to include "reasonably available sources" or similar phrasing.
    - Additionally, some particularly innovative areas of healthcare delivery do not have generally accepted or publicly available guidelines to form the basis of CDS 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 PGHD, the Patient-Reported Outcomes Measurement Information Systems (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. The FDA is encouraged to account for this gap in its CDS guidance.

        - We believe it would be helpful to provide examples of plain language for stakeholders to review and model on once the guidance is finalized.

- ***Improve the application of the International Medical Device Regulatory Forum's framework to CDS.*** We are encouraged by FDA's efforts to apply the International Medical Device Regulatory Forum's (IMDRF's) framework to risk-based policy for CDS software functions. However, as drafted, the method by which the IMDRF framework is incorporated into the draft CDS guidance may cause confusion with the scope of the statutory exclusions set forth in 21CC. The FDA's position with respect to the exemptions of low risk software are narrow and do not sufficiently exclude low-risk software from its regulation. Further, particular confusion may be caused by (1) introducing definitions not in U.S. law ("critical" "serious," and "non-serious"); (2) presenting IMDRF categories addressing the significance of information for a SaMD function that are similar and appear to overlap (e.g., "inform" and "drive"); (3) inadequately accounting for levels of CDS' autonomy and ability to continuously learn; and (4) having asymmetrical content in Tables 2 and 3 in the draft CDS guidance (e.g., Table 2 shows an "Inform x Critical" as being a Level II, but Table 3 shows that "Inform x Critical" may not even be a regulated device; similarly a Table 2 "Inform x Serious" is a Level I, but Table 3 indicates it may be subject Oversight Focus. Readers may be confused that a "Level I" product is subject to Oversight, but a "Level II" product might not be regulated at all.). CHI recommends that FDA clarify that its application of the IMDRF framework applies only to the extent that it is consistent with U.S. law (namely, the FD&C Act).
    - FDA should clearly differentiate between "inform" and "drive," which has major implications for those using FDA's guidance to determine if and how CDS software is regulated. For example, we cannot agree with FDA that software identifying early signs of disease for patients "drives", instead we believe that it "informs." Based on FDA's proposed application of the IMDRF factors, software that aids in treatment or diagnosis would be considered to "drive" clinical management and would be treated as a device. The proposed exclusion of the IMDRF concept of "driving" clinical management from "support or providing recommendations" potentially conflicts with Cures criteria. If FDA is going to incorporate the IMDRF Framework factors, at minimum the agency should explicitly confirm that "support or provide recommendations" does not constitute "driving clinical management."
    - CHI requests clarity on "inform[ing] clinical management," specifically on the meaning of what "trigger[ing] an immediate or near term-action" means. We recommend that this phrasing represent an intended and direct order for immediate action. Further, "inform" should be clarified to represent that the software function is not necessary (*e.g.*, tools to streamline workflow). Examples in FDA's CDS software guidance should provide illustration of this definition.

- Further clarity should be provided by FDA on "driv[ing] clinical management" to provide that "driv[ing]" functions are not intended to substitute for a medical professional's clinical judgement.
- CDS software under the "diagnose and treat" category should be limited in scope to CDS software used as the only basis for taking direct clinical action (in other words, the CDS software is intended to substitute in for a medical professional's clinical judgement).
- CHI requests that FDA provide further details regarding healthcare situation/condition categories, particularly between "serious" and "critical" conditions.
- CHI urges FDA to treat consumer- and patient-facing CDS in the same manner in which CDS is used by a healthcare provider. We believe this approach will provide needed simplicity to FDA's approach to CDS software. We also recommend that FDA appropriately defer to existing guidance as needed to ensure that stakeholders are clear on that guidance's continued application (e.g., FDA's wellness product guidance).

- ***Enable the use of real world evidence.*** CHI supports FDA's approach to CDS software including the concept of thoughtful design, including the design of Artificial Intelligence (AI) systems in healthcare to be informed by real-world evidence (RWE) that will promote human-centered design and usability principles as well as end-user needs. FDA should explicitly support the use of RWE in its CDS software guidance.
- ***Squarely address artificial intelligence and machine learning.*** AI and machine learning have incredible potential to improve treatments and patient outcomes, including through CDS software. CHI urges 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 FDA directly addressing AI and machine learning in this guidance – even if FDA merely indicates that it intends to address AI and machine learning in a future standalone guidance.
- ***Further clarity and guidance on explainability of CDS software.*** CHI appreciates FDA's draft guidance stating that the explainability of CDS software algorithms must reflect different approaches and levels of understanding, and we urge FDA to note that explainability of CDS software algorithms may need to be approached differently depending on its audience. Recommendations on aspects

of explainability (and levels of detail) for healthcare providers, patients, etc., is requested.

  - Further, CHI reiterates that countless CDS software innovations may 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 healthcare 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 appreciates and support FDA's clarification that "[i]n order to describe the basis for a recommendation, regardless of the complexity of the software and whether or not it is proprietary, the software developer should describe the underlying data used to develop the algorithm and should include plain language descriptions of the logic or rationale used by an algorithm to render a recommendation" in lines 254-257. However, the CHI encourages the FDA to limit the description of technical requirements to those reasonably possible.

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

  - Examples of CDS software functions that are not devices and device CDS functions that remain devices provided by FDA will be heavily relied upon by our community. We strongly urge FDA to ensure that its featured use case examples illustrate the range of technologies the CDS guidance impacts. As drafted, FDA's examples only address use cases involving the use of sensors and images. Without further examples of other CDS use cases, FDA's guidance may cause confusion as to the scope of its guidance and its application to the range of CDS software applications. We also believe stakeholders would benefit immensely if FDA included as much rationale as possible to explain why each example is considered a medical device.

- FDA examples should cover the use of CDS software for prevention purposes. As noted above, CDS software holds incredible potential to prevent, as well as treat, disease.
- Examples should address CDS software that matches disease symptoms between a particular patient and other patients, informing the patient's decision to seek diagnosis and treatment.
- Consistent with the four-factor test established in section 520(o)(1)(E)[5], CHI recommends adding the following to the category of CDS software that is exempt from FDA regulation:
  - "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."
- Building on our recommendations above regarding the scope of a "physiologic signal," we note that FDA proposes the following as an example of device software functions that are not CDS on which FDA intends to focus its regulatory oversight: "Software intended to analyze or interpret laboratory test or other device data and results to flag patient results based on specific clinical parameters (e.g., out of range test results where the reference ranges are predetermined by the lab) provided that the analysis performed by these software is not intended for immediate clinical action and does not represent a unique interpretation function but rather summarizes standard interpretation of individual variables that healthcare practitioners could do themselves." CHI believes that this example is instead better placed under the category of Non-Device CDS Functions because the function is processing test results just processed, and meets the fourth Section 520(o)(1)(E) requirement.

- ***Support for Center for Devices and Radiological Health (CDRH) collaboration with the Center for Drug Evaluation and Research (CDER)***.

  CHI applauds 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 FDA's proposal to ensure FDA-compliant recommendations on the use of a prescription drug is not considered a medical device.

[5] 21 U.S.C. § 520(o)(e)(1).

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

Sincerely,

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