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FDA-2017-D-6569

VIA ELECTRONIC SUBMISSION

December 20, 2019

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

Re: Docket No. FDA-2017-D-6569: Clinical Decision Support Software: Draft Guidance for Industry and FDA Staff

Dear Sir or Madam:

The Combination Products Coalition ("CPC")[1] welcomes the opportunity to offer comments on FDA's re-issued "Clinical Decision Support Software: Draft Guidance for Industry and FDA Staff" (hereinafter the "Draft Guidance").

We want to start by expressing appreciation for FDA moving from an approach that was not risk-based in the prior clinical decision support ("CDS") software guidance draft, to one that is. That is a change in a positive direction. We understand that many organizations recommended, in response to the prior draft of the CDS guidance, that FDA do this, and we appreciate FDA listening to those comments. That is to FDA's credit.

We hope that, as FDA finalizes its guidance, the Agency will consider our comments as the cumulative voice of industry subject matter experts who are embarking on the design and development of many innovative products that include, or integrate with, software. We further hope that FDA will leverage these collaborative views to provide a fit-for-purpose yet consistent guidance (rather than requirements) for CDS software functions that helps facilitate timely dissemination of digital health technologies to patients.

[1] The CPC is a group of leading drug, biological product, and medical device manufacturers with substantial experience and interest in combination product issues. One of our top priorities is to work collaboratively with FDA on issues affecting combination products to advance our common mission: providing the best possible health care to patients. Our diverse, cross-industry membership permits the CPC to bring a special, broad and unique perspective to these issues.

To move toward this objective, the CPC recommends that FDA revise the Draft Guidance to:

1. Apply the same regulatory framework to software regardless of the legal manufacturer;

2. Exclude from regulation more software as low risk;

3. Not limit the scope of the statutory transparency exclusion found in the 21st Century Cures Act ("Cures Act") to only software which, in the IMDRF terminology, merely informs or provides options regarding clinical management of patients;

4. Not limit its enforcement discretion to only patient-directed software that informs clinical management for non-serious situations or conditions; and

5. Clarify, with more explicit discussion and specific examples, the level of software description needed to allow intended users to independently evaluate the basis for the software's recommendation.

Below, we present our major observations, concerns, and recommendations surrounding the five proposed areas for revision listed above.

1. FDA should apply the same regulatory framework to software regardless of the legal manufacturer

The scope of the Draft Guidance excludes CDS associated with prescription drugs, drawing a distinction between drug sponsor-owned software and third-party software. This approach results in artificial categorization of software produced by a third party as inherently lower risk than software developed by or on behalf of drug sponsors. This has significant potential to disincentivize digital health innovation among drug sponsors as it disproportionately increases the regulatory burden on drug sponsors developing software for use with prescription drugs.

The CPC strongly recommends that FDA apply the same regulatory framework for CDS regardless of who disseminates it. FDA should not implement different regulatory policy for the exact same software disseminated by different entities.

It would also be helpful to understand how the Draft Guidance relates to or aligns with FDA's other digital health initiatives, including the Agency's proposed framework on prescription drug-use-related software ("PDURS").

2. FDA should exclude from regulation more software as low risk

Again, we want to express our appreciation for FDA moving from an approach that was not risk-based in the prior CDS guidance draft, to one that is.

But at the same time, we need to observe that FDA took a very small step in this direction. We understand that prior comments recommended that FDA go much further to exempt other low risk software. For example, in comments submitted by the CDS Coalition on February 5, 2018, that coalition specifically recommended that the Agency use the IMDRF framework for risk

stratification, and extend the exemption of low risk software to all software that merely informs clinical management and is considered to be of low impact. In appendix A to those comments, the CDS Coalition included a list of 22 low risk software products already on the market (falling into three subcategories)[2] that the coalition recommended be exempt.

In its newly revised CDS guidance, FDA only extends the exemption to products in one[3] of those three subcategories, which has the effect of exempting only one out of the 22 products listed in that appendix A. That is a very small step indeed. And the Agency offers absolutely no justification or explanation as to why the subcategories that contain the other 21 products should not be exempt.

We think it is incumbent upon FDA to explain, in a data-driven manner, why exactly the Agency is drawing the line where it proposes. There should be data underlying FDA's decision, and it would help the public discourse if FDA identified those data so that they could be discussed. FDA's policymaking should be both data-driven and transparent. Otherwise we are left with arbitrary distinctions built on opinion. Exempting one product category out of 22 proposed in the CDS Coalition comment letter is not a meaningful improvement. In other words, the change did not truly produce a risk-based approach when the only exclusion is de minimis.

3. FDA should not limit the scope of the statutory transparency exclusion found in the Cures Act to only software which, in the IMDRF terminology, merely informs or provides options regarding clinical management of patients

The Cures Act specifically provides that software "intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition" falls within the scope of the statute's transparency exclusion, provided the other three delineated criteria are met. Despite this statutory language, and in conflict with what appears to be Congress's intent, FDA takes the position in the Draft Guidance that software functions that "drive clinical management" are not CDS, and thus could not fall within the statute's transparency exclusion.

In advancing this position, FDA starts, in Section VI.A.2. of the Draft Guidance, by reciting the IMDRF definition of "driving clinical management," which characterizes this software function as one that provides information that will be used to "aid in treatment by providing enhanced support…, aid in diagnoses, [or] to triage or identify early signs of a disease or condition…to guide next diagnostics or next treatment interventions." FDA goes on to assert that because software

[2] These subcategories included: (1) SaMD that provides information to drive clinical management of a disease or conditions in a non-serious situation or condition is a Category I and is considered to be of low impact; (2) SaMD that provides information to inform clinical management for a disease or conditions in a serious situation or condition is a Category I and is considered to be of low impact; and (3) SaMD that provides information to inform clinical management for a disease or conditions in a non-serious situation or condition is a Category I and is considered to be of low impact.

[3] This is the third subcategory listed in the footnote directly above (SaMD that provides information to inform clinical management for a disease or conditions in a non-serious situation or condition is a Category I and is considered to be of low impact).

functions that drive clinical management "go beyond *supporting or providing recommendations*" (emphasis added) to a health care professional, and are instead "relied on to *guide* next diagnostics or treatment interventions" (emphasis added), they are not CDS, and therefore, could not fall within the scope of the Cures Act transparency exclusion.

Given the synonymous nature of the words "recommend" and "guide," there appears to be little basis for the distinction FDA is making between software that *provides recommendations* with regard to healthcare decision-making (which may fall within the scope of the statutory exclusion) and software that *guides* such decision-making (which, based on FDA's reasoning, could not fall within the scope of the statutory exclusion). Further, we note that the Draft Guidance expressly defines the "driving clinical management" function to include the provision of information to "aid" in health care professional decision-making (including, specifically, "aid[ing] in treatment by providing enhanced *support*" (emphasis added)), which tracks extremely closely with the language from the third criterion of the Cures Act transparency exclusion referenced above describing software functions that "support" health care professional decision-making.

As we believe FDA's position here— that software functions that "drive clinical management" are not CDS that could fall within the scope of the Cures Act transparency exclusion — conflicts with the plain language of the Cures Act, we ask that FDA revise the Draft Guidance to appropriately align with the statute and ensure appropriate deference is given to Congress's intent.

4. FDA should not limit its enforcement discretion to only patient-directed software that informs clinical management for non-serious situations or conditions.

In the original draft CDS guidance, FDA proposed to extend enforcement discretion to CDS software directed at patients or caregivers (rather than healthcare professionals) that, in general, meets the definition of exempt CDS software for healthcare professionals under the Cures Act. The Agency, however, noted that this is not open-ended because it means, among other things, that the "kinds of explanations that a healthcare professional may be able to understand and apply are different than the kinds of explanations that a patient may be able to understand and apply, given the differences in clinical education and experience." That observation greatly reduces the potential candidates of software that may be exempt when directed to patients.

But now, without explanation, FDA retreats from that position. Starting on line 309, FDA now proposes:

> "FDA considers such Device CDS functions, which are intended for patients or caregivers to inform clinical management for non-serious health care situations or conditions (i.e., inform x non-serious), to be low risk when the CDS function is intended for a patient or caregiver using the device to be able to independently review the basis for its recommendations. … The recommendation for the type of decision to prevent, diagnose, or treat should be the type of decision a patient or caregiver would routinely make without the input of a health care professional, and the data used by the CDS function and the basis for its recommendations would be of a kind that patients or caregivers understand."

That passage adds significant limitations to the previously proposed enforcement discretion affecting patient-directed software. Under the newly proposed language, the use would have to be low risk and the recommendation would have to relate to a type of decision "routinely" made without a doctor's input.

Additionally, the Draft Guidance could potentially move a significant number of software functions/mobile apps currently falling under FDA enforcement discretion to the focus of FDA's regulatory oversight. For example, self-configured medication reminder apps like the Medisafe Pill Reminder may now become the focus of FDA's regulatory oversight as they would fall in the "Inform x Serious" category while being intended for patients who cannot independently evaluate the basis for the software's output from the information provided in the app.

The CPC strongly recommends that FDA align the language referenced above in the Draft Guidance with that in the Cures Act. More broadly, FDA should harmonize regulation of software functions in its various guidance documents and Agency-wide.

5. FDA should clarify, with more explicit discussion and specific examples, the level of software description needed for intended users to independently evaluate the basis for the software's recommendation

The CPC is concerned about the lack of clear guidance regarding the nature and scope of the description of the software or Machine-learning ("ML") algorithm within the software user interface ("UI") needed to enable users' independent evaluation of the basis for the software's recommendations. This concern is critical as there are no precedent or established industry benchmarks for disclosure of such information, and the ability for users to independently review the basis for software recommendations is a key criterion for falling within the Cures Act transparency exclusion. We also believe that, in some cases, there may be legal concerns with such disclosures when entangled with proprietary information.

The CPC requests that the final guidance document include more explicit discussion, including specific examples, about the level of software description needed within an app to enable independent review and evaluation of the software output. It would also be helpful to know if the "plain language" descriptions FDA refers to in the Draft Guidance (line 256) are intended to refer to the Federal Plain Language Guidelines[4] published in 2011 following the Plain Writing Act of 2010. If that is the case, it is important to note the need for updating the referenced Guideline documents to include software-related information and examples in accordance with current innovative technologies.

[4] *Available at* https://www.fda.gov/media/85771/download.

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We appreciate the opportunity to provide input on the Draft Guidance and are happy to meet with the Agency to clarify or discuss any of our suggestions.

Yours truly,

Bradley Merrill Thompson,
On behalf of the Combination Products Coalition