

FDA Webinar: Clinical Decision Support Software: Draft Guidance

**Moderator: Irene Aihie
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Coordinator: Welcome. Thank you everyone for standing by. Participants over the phone lines are in a listen-only mode until the question-and-answer session of today's event. Now at that time you may press star 1 on your touchtone phone to ask a question. Today's conference is being recorded. If you have any objections, you may disconnect. Now I'd like to turn the call over to your host, Ms. Irene Aihie. And thank you ma'am. You may begin.

Irene Aihie: Hello and welcome to today's FDA Webinar. I am Irene Aihie of CDRH's Office of Communication and Education.

On September 27, 2019, the FDA issued a draft guidance document on Clinical Decision Support Software. The purpose of this draft guidance is to describe the FDA's regulatory approach to Clinical Decision Support Software function.

The agency's approach includes recent changes to the FD&C Act made by the 21st Century Cures Act which amended Section 520. And excludes certain software functions from the device definition.

Today Bakul Patel, Director of the Division of Digital Health, and Matthew Diamond, Medical Officer in the same division, both here in CDRH, will present an overview of the draft guidance document.

Following the presentation we will open the lines for your questions related to information provided during the presentation. Additionally, there are other center subject matter experts here with us today to assist with the Q&A portion of our Webinar.

Now I give you Bakul.

Bakul Patel: Thank you Irene. And thank everybody on line for joining us today on this Webinar for our Clinical Decision Support Software Guidance that we just published in September.

Before we get started, I'm just going to start with a brief overview on what we're trying to achieve today as objectives for this Webinar.

We want to share our current thinking on Clinical Decision Support Software including functions that are considered devices. We also want to explain our FDA's risk based approach to CDS software function that still remains divisive.

Before we get into that, let me just give you sort of the topics we want to cover today. We're going to share with you the background on what the 21st Century Cures Act has done to the law. And we want to highlight the changes that we are presenting in this draft guidance, from the previous draft that we had published.

We're going to share a little bit details into what the background is in terms of how we came to this point. And then we'll follow with questions and answers.

So let me just take us back to the very beginning where we started this journey on understanding the risks of the product itself, rather than focusing on the platform of the product.

So we used this model and this framework to base our policy decisions on the risk of the product. Focusing on the software functionality and, focusing on those things that are higher risks to patients. Which allows us to give us platform independence and promote innovation while balancing the patient safety aspects of this software and the usefulness in promoting patient engagement.

Here is what 21st Century Cures Act builds on our existing framework of digital health policies. We are recognizing where products are low risk, quantify some of the practices that we have been publishing, and applying a very pragmatic and more practical, least burdensome approach towards device circulation.

To give you an overview of what 21st Century Cures Act has put forth, it covers five different things. But today we're going to talk about only one thing.

The five things - I'll just touch on it very briefly. In 2014 we published a FDASIA Health IT Report which talks about the various categories of health IT software that can exist. And Cares Act takes that and says that administrative support software that was identified in the Health IT Report is no longer divisive.

We had general wellness policies. We had health management functionalities that is the electronic patient records and electronic health records that were identified in the Health IT Report as well. And the Cures Act qualifies those policies and the work that was done in 2014, and says they're not divisive.

Let me - we also had other policies such as medical device data systems and general wellness which were also qualified in the 21st Century Cures Act.

I'm not going to go over all the details of the Act itself or read this slide. But just to highlight those four points and the four criteria that Cures talks about in the last provision of Clinical Decision Support is, the acquisition of the signal of the body. We will talk in detail about that.

I will hand you to Matthew who will explain in detail the functions of displaying and analyzing. But just simply printing medical information.

And the third and the fourth criteria about where the Act describes when proper functions would be excluded from the device definition and, when it would not be.

So the Cures Act does not actually consider blood transfusion of blood CBER related products to be excluded from the medical device definition itself.

However, as we dive deeper into this, it will be further clear about when it is a medical device or, when a software function is a medical device, what would that mean.

So this - to take you from where we were in - when the previous draft guidance to today, on December 8, 2017 we published the draft guidance on Clinical and Patient Decision Support.

We asked for clarity and we got them. We heard the feedback loud and clear. So today we are going to go over the reissuance of the draft guidance which is in response to the comments received from the industry and the stakeholders that commented on this guidance.

We understand it's a very important guidance and we need your feedback again. We are now seeking the second round of public comment. And we're hoping that we address most of the comments that we received the first go around. And we can get this policy to a place where it really balances out patient safety and allows a very practical approach towards this amazing technology and the solutions that are being brought to the market.

With that let me just give you Matthew Diamond, the Medical Officer in my division. And he's going to cover into detail about what the guidance actually entails.

Matthew Diamond: Thank you Bakul. It's a pleasure to be here speaking today about Clinical Decision Support Software and specifically, the draft guidance that we recently released.

And I'm going to begin by highlighting some of the changes from the previous draft CDS Guidance in this new draft.

Number one is the use of a risk-based approach for the regulation of device CDS, as we've alluded to already, informed by the International Medical Device Regulators Forum or IMDRF.

Number two is that we are no longer proposing to use a separate category for Patient Decision Support Software. And rather, the intended user of the CDS, whether they are a healthcare professional or a patient or caregiver, is taken into account in the risk-based framework for CDS.

And number three is that we're providing additional clarification in the interpretation of the four Cures criteria that we just introduced, that excludes certain CDS from device definition.

Now we've mentioned the risk-based framework from the International Medical Device Regulators Forum or IMDRF. And here we are briefly showing some information from that IMDRF framework. Many of you will recognize the three by three matrix at the top of this slide, both from the IMDRF documents and Table 2 of the draft CDS Guidance.

I'm going to use this slide here just to mention now the two primary criteria identified by IMDRF to risk stratify Software as a Medical Device. The first is the criticality of the healthcare situation or condition, ranging from non-serious, to serious, to critical.

And the second is the significance of information provided by the software to the healthcare decision, ranging from just informing the user, to driving clinical management, to actually performing the treatment or diagnosis.

There are a lot of details on this slide that we're not going to get into right now. You'll see these tables later in the presentation, and you can use them as a reference.

Their purpose here is to re-introduce the IMDRF categorization scheme and bookmark these tables for later. And it's probably worth defining the term, SaMD or Software as a Medical Device, which this framework is focused on.

This is what might previously have been colloquially called Standalone Medical Software. It is software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

And I would also like to take a moment to define Clinical Decision Support. It is a tool or a collection of tools that provide healthcare professionals and patients with knowledge and person-specific information intelligently filtered or presented at appropriate times to enhance health and healthcare.

It includes computerized alerts and reminders for providers and patients, clinical guidelines, condition-specific order sets, patient data reports and summaries, documentation, templates, and diagnostic support.

Okay, now that we've completed the background section of this Webinar, we're going to dive into the details of the draft CDS Guidance itself. Remember, the purpose of this draft CDS Guidance is to describe FDA's potential regulatory approach to CDS software functions, including the changes to the FD&C Act made by the Cures Act and the IMDRF risk framework, both of which you've been introduced to by now.

Remember that the draft CDS Guidance is not final, nor is it in effect at this time. The software provisions of the 21st Century Cures Act that modified the FD&C Act that defines a medical device, though, are self-implementing and in effect.

I think it's worth pausing here for a moment to summarize at a high level, the things to consider when thinking about the regulatory status of CDS software. First we ask whether a CDS product or function meets the definition of a device.

And second, among those products or functions that are devices, we ask whether it is the type of device on which FDA intends to focus its regulatory oversight.

Or on the other hand, whether it is a sufficiently low risk device that it is not the focus of our regulatory oversight, but rather FDA intends to exercise our enforcement discretion.

And it is that first consideration, device versus non-device, that is based on the regulations. And specifically, the Food, Drug, and Cosmetic Act and the way that was amended by the 21st Century Cures Act.

The second consideration is based on FDA policy that leverages the IMDRF framework for medical software, which we've mentioned and will review in more detail shortly. It will be helpful if you keep these two considerations in mind during the rest of the presentation.

First, device or non-device. And second, is a device the focus of our regulatory oversight or, is it under enforcement discretion?

The first area we're going to focus on is the criteria to determine whether CDS software meets the definition of device. And here is a summary table, which appears as Table 1 in the draft CDS Guidance, of those criteria for device CDS versus non-device CDS.

To be non-device CDS, a software function must meet all four criteria from Part E, which we mentioned previously. Only CDS software functions that are intended for healthcare professionals, and for which the user can independently review the basis for the recommendation provided by the software, can be excluded from device definition by the Cures Act.

And how about device CDS? To be device CDS, software must meet the first two criteria of Cures and part of the third criteria. In other words, it must be intended for displaying, analyzing, printing medical information, but not for analyzing or interpreting a signal or medical image. And it must be intended for use by their patient or caregiver.

Or if intended for use by a healthcare professional, that healthcare professional would not be able to understand the basis for the recommendation by the software.

I think it's worth mentioning here that besides the type of non-device CDS that meets all four criteria of the Cures Act, there are other types of non-device CDS. These are software functions that FDA has traditionally considered CDS but never considered device functions. For example, software that presents best practices in an institution or facilitates access to treatment guidelines.

So we've introduced the four criteria from the Cures Act, that if a software meets all of them, then that software is considered non-device CDS. Let's now go into more detail about each of the four criteria.

Criterion 1. The software function must not be intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system.

In other words, software functions that acquire a process or analyze a medical image or signal are not excluded from the device definition by the Cures Act. We generally consider physiological signals to include those signals that require use of either an in vitro diagnostic device or a signal acquisition system that measures the parameter from within, attached to, or external to the body for a medical purpose.

These systems often include the use of sensors, collections of samples, or specimens, or the use of radiological imaging systems.

Let's say a little bit more about physiological signal acquisition systems. Presently, many physiological signal acquisition systems are intended to monitor physiological signals for medical purposes and therefore are considered medical devices.

But some physiological signal acquisition systems are not a device. And those include, for example, activity monitors that measure physiological parameters not specifically intended or marketed for a purpose identified in the device definition.

And, software functions that measure physiological parameters for purposes of biometric identification such as retinal image analysis for secure access to a facility are also not devices.

We encourage manufacturers to engage with the FDA if a physiological signal acquisition system previously only considered for a medical purpose is intended to be used for a non-medical purpose.

So to summarize, software functions that acquire, process, or analyze a medical image or signal do not meet Criterion 1. And are not considered CDS. And are not excluded from the device definition by the Cures Act.

Okay, let's move on to Criterion 2. Criterion 2, the software function must be intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information. For example, demographic information, symptoms, test results, medical device output such as heart rate or blood pressure, patient discharge summaries, or medical information such as clinical practice guidelines, peer reviewed clinical studies, textbooks, approved drug or medical device labeling, and government agency recommendations.

FDA interprets this to include software functions that display, analyze, or print patient specific information. And in general, this is the kind of information used by the intended user to make decisions about prevention, diagnosis, or treatment of a disease or condition for an individual patient.

Let's move on to Criterion 3. The software function must be intended for the purpose of supporting or providing recommendations to a healthcare professional about prevention, diagnosis, or treatment of a disease or condition.

Software functions that meet this criterion are evidence-based tools to support a healthcare professional's decision-making. They inform treatment options or a diagnostic test for a patient. They can accomplish this by collating or developing recommendations based on an analysis of patient-specific information to a healthcare professional who may then use this information to make a decision about the care of a patient, along with other information and factors of which the healthcare professional is aware.

This aligns with the Inform category of the IMDRF framework, which we'll talk about more in a moment. It does not treat a patient, determine a patient's treatment, or provide a definitive diagnosis for a patient.

Note that software functions that meet the first two Cures criteria, but support or provide such recommendations to patients or caregivers, rather than to healthcare professionals are CDS and remain in the device definition. They are device CDS.

Okay, we have one criterion left. Criterion 4 says that the software function must be intended for the purpose of enabling a healthcare professional to independently review the basis for such recommendations that such software presents, so that it is not the intent that the healthcare professional rely primarily on any recommendation to make a clinical diagnosis or treatment decision regarding an individual patient.

FDA interprets this provision to mean that manufacturers of non-device CDS should describe their software functions in clear language including the purpose or intended use of the software function, the intended user, the inputs used to generate the recommendation, and the basis for rendering a recommendation.

The description of the basis for rendering a recommendation includes a plain language description of the logic or rationale used by an algorithm, the underlying data used to develop the algorithm. Also the sources supporting the recommendation or the basis for the recommendation should be identified and available to the intended user and understandable by the intended user.

The draft guidance states that this is regardless of the complexity of the software and whether or not it is proprietary.

A practitioner would be unable to independently evaluate the basis of a recommendation and therefore would be primarily relying upon it if the recommendation were based on information whose meaning could not be expected to be independently understood by the intended healthcare professional user, for example, if the inputs used to generate the recommendations are not identified.

Okay, so we've gone through the four criteria for CDS to be excluded from the definition of device by the Cures Act. Next we're going to focus on the subset of CDS that is not excluded from the device definition. In other words, we're going to focus on device CDS and look in more detail at the risk framework that the draft guidance describes as being used to risk stratify Software as a Medical Device, or SaMD.

Here again, those of you who are familiar with the IMDRF risk framework for SaMD will recognize this three by three matrix that shows the two most significant factors for risk stratifying SaMD.

One factor is along the Y axis. The criticality of the healthcare situation or condition, from least critical, called non-serious, at the bottom, to most critical at the top.

The second factor, the significance of information provided by the software to the healthcare decision goes from lowest significance on the right side of the chart to the highest significance on the left side.

So taken together, the lowest impact or lowest risk SaMD is generally on the lower right corner of this representation. And it increases in the impact or the risk of the SaMD moving up to the upper left corner.

Please don't ask why it increases from right to left rather than from left to right like a standard Cartesian coordinate system. That's just the way the figure was depicted in the IMDRF documents.

When thinking about that second factor, the significance of information provided by the SaMD, which you could think of as being the role the SaMD plays in the healthcare situation, the lowest impact or lowest category within this factor is the informed category, which is on the right side of the three by three matrix, and it's highlighted here in blue.

And this is where CDS functionality live. In other words, CDS functions inform clinical management. In and of themselves they do not drive clinical management, and they do not treat or diagnose. But they can inform clinical management through the full spectrum of criticality, from non-serious to critical.

Let's try to describe in words what this inform really means. Here we have the two factors for risk stratification of SaMD that we just mentioned, in the two columns, with the significance of information being on the right and with the lowest significance category being at the bottom of that rightmost column.

Here again, the informed functionality is highlighted in blue. Informed means to inform of options, or to provide clinical information by aggregating relevant information.

It means the software is intended to provide information such as treatment or diagnostic options or aggregating clinical information that may support a recommendation to a healthcare professional, patient, or caregiver. Informed functions do not trigger an immediate or near-term action. CDS functions are inform functions.

Let's now zoom in on this third column in the IMDRF three by three matrix, the inform functionality. And we will examine a table that was provided in the guidance that identifies how the IMDRF framework, along with the Cures criteria, can be used to identify first of all, whether a CDS software function is a device. And then if it is a device, whether it is the subject of FDA's oversight focus.

And here is a table that is very similar to Table 3 that is provided in the draft CDS Guidance. This is meant to represent CDS software functions. So essentially, the inform software function. And includes the full spectrum of criticality with the IMDRF category labeled in the column on the left. From least critical at the bottom, that's inform non-serious, to a higher criticality in the middle, that's inform-serious, to the highest criticality at the top, that's inform-critical.

From here we move to the second column and ask whether the function is intended for the purpose of enabling the user to independently review the basis for the recommendation, so that it is not the intent that users rely primarily on any such recommendation, which is part of Cures Criterion 4.

So for each of the IMDRF categories, we have software of that category that the user can independently review the basis for, and software of that category that they cannot.

And finally, we have separated out the SaMD further, on the basis of who the user is. So the third column contain SaMD intended for use by healthcare professionals. And the fourth column contains SaMD intended for use by patients or caregivers.

You'll see that enforcement discretion appears twice in this table. We've mentioned enforcement discretion, but I would like to define it specifically.

Enforcement discretion indicates that at this time, and based on our current understanding of the risk of these devices, FDA does not intend to enforce compliance with the applicable device requirements, including but not limited to registration and listing, premarket notification, post market reporting, and quality system regulation.

This table depicts regulatory oversight of CDS. That includes both device CDS and non-device CDS. So in order for a software function to make it into this table it already has to meet the first two criteria and part of the third of Cures, namely that it is not intended to analyze a medical signal or image, but rather it displays, analyzes or prints medical information, and serves an informing purpose as defined by IMDRF, that we've discussed.

Let's start by reviewing this chart and focusing on software intended to be used by a healthcare professional. Here is a summary of the risk-based policy for CDS intended to be used by a healthcare professional as the intended user, utilizing the IMDRF framework.

And you will see that in general, if a software function has a healthcare professional as the intended user, and if that healthcare professional can independently review the basis for the recommendation as we previously discussed, then it is excluded from the device definition by the Cures Act.

These types of software are highlighted in this slide in yellow. If the user can independently review the basis for the recommendation, that CDS is not a device. And this is across the full spectrum of criticality for the SaMD within the informed category of SaMD for inform non-serious, inform serious, and inform critical.

Among the remaining types of SaMD on this chart, wherever the answer to the question of whether the user can independently review the basis for the recommendation is no, then these are medical devices. And it is among these medical devices that we can use the IMDRF framework to determine regulatory oversight for these device CDS functions.

If the healthcare situation or condition of the SaMD is critical or serious, then these SaMD will be our oversight focus. And these are depicted in dark blue on this slide.

However, for the lowest criticality of the SaMD, the informed, non-serious category, FDA will exercise enforcement discretion for these device CDS functions, and it does not, at this time, intend to enforce compliance with applicable device requirement. This category is colored in orange.

Let's provide some examples. And these are taken directly from the guidance. Both of these examples fall into the informed critical category of CDS. At the top is an example of software which is our oversight focus. Specifically, a machine learning algorithm for which the logic and inputs are not explained that identifies hospitalized, Type 1 diabetic patients at increased risk of post-operative cardiovascular events.

This software is a device CDS function because the healthcare practitioner is not expected to be able to independently evaluate the basis for the software's recommendations.

The FDA intends to focus its regulatory oversight on this software because it is intended to inform clinical management for a critical situation or a condition.

A related example is described right below it, which is similar to the first example. But in this case the healthcare professional could evaluate the basis of the software's recommendations because the logic and data inputs for the machine learning algorithm and criteria for risk of cardiovascular events were explained and available to the healthcare professional.

In this second example this software would be considered non-device CDS and is therefore not a device.

Let's move on to discuss CDS software intended to be used by a patient or caregiver. The risk-based policy for this type of CDS is summarized in this slide.

Again here note that the first column on the left identifies the category of SaMD, from the least critical inform non-serious on the bottom, to the inform critical on the top.

The second column asks whether the user can independently review the basis for the recommendation, as we've discussed. And the third column shows the regulatory oversight of this type of SaMD.

Since all of this software is intended to be used by a patient or caregiver rather than by a healthcare professional, then it is not excluded from the device definition by the Cures Act. That's why all of these CDS software functions are device functions. You don't see any yellow on this slide like you saw on the previous slide.

Now, among these categories of device CDS, for the lowest category, informed non-serious, for which the lay user can independently review the basis for the recommendation, the FDA will exercise enforcement discretion for these device CDS functions, and it does not, at this time, intend to enforce compliance with applicable device requirements. This category is colored in orange.

The remaining patient or caregiver oriented device CDS are within FDA's oversight focus and depicted here in dark blue.

We'll provide here two examples of device CDS with the intended user being a patient. Both would be considered to be in the informed non-serious category of the IMDRF framework. These examples are also both taken directly from the guidance.

At the top is an example of software which is our oversight focus. It is intended for patients and providers, and it provides a questionnaire to assess the patient's level of stress and anxiety, prior to any diagnosis of general anxiety disorder, and recommends treatment options based on the output of the assessment.

This software is a device CDS function because it is intended for patients and to inform clinical management.

The FDA intends to focus its regulatory oversight on this software because it is intended to inform clinical management for our non-serious situation or condition. But the patient is not expected to be able to independently evaluate the basis for the software's recommendations.

The second example is similar to the first. But the patient could understand the software's recommendation. The software provides the basis of its recommendation that is understandable to the patient, of how the questionnaire assesses stress and anxiety, and how the recommendation is based on peer-reviewed publications and/or clinical practice guidelines and the patient's answers.

This software would be considered device CDS but for which based on our current understanding of the risks of these devices, the FDA does not intend, at this time, to enforce compliance with applicable device requirements.

I'd like to remind you that there is other healthcare related software, some of which could even resemble CDS but which do not meet the definition of a device, independent of the Cures Act.

And there are many device software functions that are not considered CDS for a number of reasons, for example because they drive the clinical management rather than just informing, or because they analyze a medical signal. And the next slide will provide such an example.

We would encourage you to familiarize yourself with other software guidance, including the Policy for Device Software Functions and Mobile Medical Applications Guidance, which has many such examples.

There is a section of the guidance called, examples of device software functions that are not CDS, on which FDA intends to focus its regulatory oversight. We are presenting here two examples taken from that section. These software functions do not meet the definition of CDS because they analyze or interpret a medical signal or medical device data.

The first example is in the area of FDA's oversight focus. It is software intended to generate an alarm or an alert, to notify a caregiver of a life threatening condition such as stroke, and a caregiver relies primarily on this alarm or alert to make a treatment decision.

This software function is a device function because it is intended to analyze a medical signal and to aid in treatment. This example of an alarm or an alert that a caregiver relies on to make a treatment decision remains the focus of FDA's regulatory oversight because it is high risk.

The second example is one that is under enforcement discretion. It is software that is intended to analyze or interpret laboratory tests or other device data and results to flag patient results based on specific clinical parameters, for example, out of range test results where the reference ranges are pre-determined by the lab, provided that the analysis performed by the software is not intended for immediate clinical action and does not represent a unique interpretation function, but rather, summarizes standard interpretations of individual variables that healthcare practitioners could do themselves.

This is a device function because it is intended to analyze the medical signal, but FDA does not currently intend to enforce compliance with the applicable device requirements of the FD&C Act for this flag notification software function because it is not a unique interpretation function and it is low risk.

We would like to highlight some additional resources. The first link is the draft CDS Guidance that is the subject of this Webinar. And the second is the IMDRF framework for SaMD. Additionally, if you would like to sign up for email updates from the FDA Division of Digital Health, you can sign up using the link at the bottom of this slide.

We encourage you to submit comments on this guidance. We're in the middle of a 90 day comment period. Please submit your comments and suggestions regarding this draft guidance, as Bakul mentioned, by December 26, 2019. Here is some information about how to submit these comments.

And if you have additional questions, you can email FDA's Division of Digital Health directly at digitalhealth@fda.hhs.gov. You can always contact FDA's Division of Industry and Consumer Education or DICE at dice@fda.hhs.gov.

This presentation, the transcript, and Webinar recording will be available at the link on the bottom of this slide. Thank you very much. And we're going to open this Webinar up for your questions in a moment.

Coordinator: This is the operator. If you would like to ask a question over the telephone, please press star 1. If you muted your phone, please unmute and provide your name. Your name is needed to introduce your question.

So to ask a question now, please press star 1 and provide your name. One moment please.

Bakul Patel: Yes, this is Bakul. And I just wanted to make sure folks are ready to ask questions. I want to underscore what Matthew just mentioned about, this is a

draft guidance. We take all comments very seriously. So we encourage everybody to look at the proposal and provide us comments and suggestions.

More importantly, the framework and the application of the framework, it's really important for us to get it right. Because we understand it's a really important area for most of the folks are (unintelligible) in the space. And hopefully it will lead to a higher confidence in the users, using this type of software that folks are about to use.

So, we'll take questions now. And as the operator mentioned, we're open for those questions.

Coordinator: Our first question now from (Mike Benicki). Sir, your line is open.

(Mike Benicki): Hi Bakul and hi Matt. Thanks for your seminar today. I had a question with regard to the interface between let's say, CDRH software and CDER software. For example, it appears from this guidance, and please correct me if I'm wrong, that some products that would be originally under the enforcement discretion, under your original guidance for medical app software might be regulated now.

Like for example, let's say a self-configured medication reminder. Or let's say a self - or a medication reminder that's drug branded. I wonder how you'd comment on those.

Bakul Patel: I do - I mean as was laid out, the other policies in the Mobile Medical Apps Guidance now applies to all software. What I would say is, those policies still are in effect. Which means, the medication reminder example that you mentioned specifically, and what we had covered in the Mobile Medical Apps Guidance and Software Functions Guidance, and Software Functions

Guidance, they still remain under what we termed as, enforcement discretion. That doesn't change.

This particular guidance that we are talking about in terms of draft is covering the entire landscape of software that could potentially be used. And honing in to the areas where 21st Century Cures Act specifically said they're not devices. So that's how I would recommend you take a look at it.

In respect to the standard for drugs, I would say that there is actually a document that was proposed under - by the standard for drugs. I think that's what the alignment is going to be. But as we move further into this journey, we'll probably be having more clarification for this.

(Mike Benicki): Okay. Thank you.

Coordinator: Our next question now from (Kyle Foshee). Ma'am, your line is open.

(Kyle Foshee): Hi, thank you so much. Very helpful information today. I had a quick question. And when I was reading the draft guidance this came up. And I honestly couldn't answer this.

How can a patient independently review the basis for a recommendation? So, I'm specifically thinking about when the enforcement discretion will be exercised. I understand when it - an HCP being able to independently review the basis for a recommendation doing that analysis.

But it's not so clear to me, when a patient or how a patient could do that. Could you provide us an example?

Bakul Patel: Yes. We'll talk about that in a second. But I think the fundamental principle that Cures presents it to us for HCP was, they were able to make the right choices.

Now they may not be the same choices a patient may take on. However, if there's enough transparency, we didn't want to forego that same principle for patients as well.

So we may not have an exact example, but I can imagine in a hypothetical case, where somebody may be able to take, you know, a choice - make a choice based on the information available on a particular therapy or a particular treatment as they suggested. Or not suggested, by the product makers.

So there is a potential for this case where the software is so clear. And it's patient directed, that does not involve anything, a healthcare provider is potential a product to be transparent enough that the patients can make those choices. And they may not be the same choices a healthcare provider would make.

(Kyle Foshee): All right. Thank you.

Coordinator: Thank you both very much. Now our next question is from (Todd Shetty). Your line is open sir.

(Rod Shetty): Yes, thank you. It's (Rod Shetty). Thank you Bakul and Matthew. I think this was great. My question was already asked but, just a question for Bakul and Matthew.

Do you encourage pre-meetings with your group? Or, if like the other divisions within the FDA (unintelligible), what's the process I guess, is the question?

Matthew Diamond: Yes, thanks very much for the question. We do encourage you to come early and come often and utilize the pre-submission process to discuss the specifics of your application. And to plan especially any clinical trials or other aspects of your program.

You could also feel free to reach out to the Division of Digital Health if you would like us to be particularly involved in any of those pre-submission discussions.

(Rod Shetty): Thank you.

Coordinator: To ask a question please press star then 1. And if your phone is muted, please unmute it and record your name. Our next now from (Virginia Farrah).
Ma'am, your line is open.

(Virginia Farrah): Yes, hi. Thank you so much for the information. It was extremely helpful. My question is around, if a product was considered a CDS in the previous draft guidance, and under today's draft guidance, with the clarity around it, is no longer considered a device CDS. And it would have to go through the normal submission round, has FDA released or will they release some sort of transition plan or guidance on what to do for those cases?

Bakul Patel: Yes, without any specific examples -- this is Bakul -- I'm not sure that I would say that there is such a scenario. But I can imagine there could be a potential hypothetical scenario there.

We have gone through a lens to make sure that we haven't done so. But I do want to emphasize that the previous guidance was also a draft guidance. And this guidance is also a draft guidance. So you shouldn't - there should not be any transition period, so to speak.

However, if there is - the clarity yields to a place where we need the different discussions, like Matthew mentioned for the previous caller, I would encourage to, in those cases, reach out to the proper division or my division to discuss those specific cases.

(Virginia Farrah): Thank you.

Coordinator: Thank you. Our next now is from (Paige Hesity). Your line is open.

(Paige Hesity): Good morning. Thank you very much for this information. It was very helpful. And thank you for allowing for additional public comment.

My question is really in regards more to the machine learning devices. In the examples and how you talk about it, you state that around the logic and input being available for review by the healthcare provider.

Does that mean that it has to be available in real time, as the process or the device is working. Or if there is a process by which healthcare professionals review and sign off on the algorithms and, there is evidence and documentation for that?

Or what is being programmed is already a clinically approved protocols, either by - approved by professional organizations like the American College of Surgeons, for example? Does that still qualify for being included as a device that needs oversight and regulation or not?

Bakul Patel: I think you asked a couple of questions and I'll see if Matthew wants to add to this. But I would recommend, there is this concept of how an intended use of a particular software is achieved. Either through a fixed algorithm or through a machine learning algorithm.

I think this guidance talks and focuses really on like, what are you intending the product to do and, who is going to use it. And when it's going to be used.

So when we focus on that, the mechanism of where - how it is achieved, either in different mechanisms, does not - is not taken into consideration. Because our policies and our law basically hones in on when a product is used for certain purposes, by certain individuals. And in that context, do they have the right information to make their choices or not? So, that's the foundation of what this guidance talks about.

You asked a question about clinical practice guidelines. And then Matthew mentioned that in his talk. There is clarity already and, it's already available by American College of (unintelligible) or any specialty. If that is simply implemented in a particular software, then that kind of software is actually excluded from the device definition.

For the 21st Century Cures Act, you have to follow the criterion that it needs to meet that standard.

You asked if there was a machine learning software, what it looks like so users can understand the basis of the algorithm? So specifically for that particular type of scenario, what we had said in the guidance is, we want the users to know the rationale of how that recommendation was put forth in front of the user.

We specifically did not ask for the detailed algorithm description or the code that should be in front of the users. Because we anticipate that kind of description is probably not so useful for every user.

But I do want to take some of your concepts that you are hitting on and recommend that, you know, in your particular situation, if you feel there is a scenario that is workable, that meets the intent of the statute and intent of the principles, we would love to see your feedback and get your input on how we could use (unintelligible) examples. Or ways where you would - you as a person making this product, would be comfortable.

And you would want to take that into account, what is allowable, what is not allowable, to be transparent, and the users making those choices.

So, I'm going to turn this as an ask for you as well. As well as, hoping that we can provide clarity. Matthew, did you want to add anything to that?

Matthew Diamond: Just Bakul, to echo what you said. And you asked a lot of good questions. There are a number of different ways to meet the requirements of this statute. And there are a number of different scenarios, or you could say a spectrum.

On the one hand there may be an application that it's clear the healthcare practitioner does not understand the basis for the decision. And that type of application would clearly not meet the statute.

And you know, there are some -- and you gave an example -- of carrying out well-accepted practice guidelines, if it's done in the context of an application that's transparent about how those are executed, that would, you know, more easily be seen how it meets the statute.

And we would encourage you to communicate, both in response to this draft guidance, and also on any particular submission, about how your application achieves these goals.

Irene Aihie: We'll take our next question.

Coordinator: Thank you very much. Now our next question from (Patricia Sede Laperch).
Ma'am, your line is open.

(Patricia Sede Laperch): Thanks very much. And thank you again for the helpful information.

So it does appear very clear from the guidance and the examples provided that all software that drives clinical management is outside the scope of the CDS guidance. And so two questions following on from that.

Does FDA intend to provide additional guidance regarding SaMD that drives clinical management? And the second question, is there - do you anticipate any knock-on effects to the software level of concerns guidance? Specifically the questions regarding major level of concern and Question 4D.

Bakul Patel: Yes, I think there are great point. I think we did, in this particular guidance, honed in on that informed category and provide more clarity. I believe you're looking for further clarity in the other parts of the framework itself.

I can't promise anything right now but yes, that's definitely one of the asks that we have seen more than once from folks. And we will take that into consideration and provide further clarity as we move further.

In terms of your question regarding level of concern, we do have an effort. Right now we're looking into addressing the guidance on software to be - content of software - content of submission and pre-market software submission. And that's a work in progress. And we are hoping to provide more alignment and clarity on that effort as well.

(Patricia Sede Laperch): Thanks very much.

Coordinator: Thank you. Our next question now is from (Jason Springs). Sir, your line is open.

(Jason Springs): Thank you very much. So just had a quick clarification question on one of the earlier caller's questions.

If we're in a scenario where a healthcare provider, we're trying to determine whether a healthcare provider using an algorithm to drive a choice, either should be considered a device or should not? One of the primary criteria was, if the healthcare provider could review the data and logic. And this is - we've had a couple of calls discussing it.

Many scenarios involve time where an algorithm of either relatively simple design or some more complex model may be used, where a healthcare provider might be able to review and understand the logic, you know, given many hours to review it.

But in real clinical use, this particular algorithm, it may be impossible for a typical healthcare provider to take in 30 different inputs all at the same time and calculate them.

So I'm wondering if there's some sort of right line or suggestion around, you know, how do we think about review. And I just contrast this to when a patient or caregiver is doing the same action, the language doesn't say review it. It says, they must understand.

So I'm wondering, you know, how should we interpret the word, review? Do we mean review with the assumption that upon review, the healthcare provider understands? And is there an envisioned test for this or a way to show that the healthcare provider actually does in fact, understand the logic and data in the actual environment where the decision would be driven by an algorithm? Thank you.

Bakul Patel: Yes, I think great question. I think you're honing in on the concept of review the basis of those recommendations. But it should not be taken only in isolation, right. So review is also in the context of review, as well.

And the second part of the statute, provision, talks about reliance. Rely primarily on such recommendations.

So again, the guidance there is the fourth bullet which Matthew went over. Which talks about informing, in the IMDRF (unintelligible), it's the informed category which talks about the logic and the rationale as opposed to the code and testing and reviewing during the use of the product.

So, it is not the same. I think you can see that's where we tried to provide clarity on is, like how is it? What's the data being used and, what wasn't used to develop the algorithm? And it could be the logic and the rationale, as opposed to the logic and the algorithm logic - base logic. So that's where we are trying to get to.

But I think as you're sort of pointing out, our proposal is those four bullet points. And how we think a user, in the context of where it's going to be used, can provide - can understand our - understand how much to rely on or not to rely on, the recommendations made.

Coordinator: Thank you. Our next question now from (Sema Palawel). Ma'am, your line is open.

(Sema Palawel): Hi. I had a question about the device which is not - I'm saying device because I'm assuming it's a device. But it's not used on patients, as such. It's used on normal population to detect any eventual disease diagnosis. So it's just a normal population which goes to the physician.

And it's through the physician but it's a normal population and they get like an advanced warning of you could be getting this disease eventually. Or maybe eventually, and the physician decides like, not (unintelligible) person. So, would that be considered a device?

Bakul Patel: So specifically today, I don't know whether I can give you an answer off the top of my head, whether that exact example would meet the definition of device or not a device.

I think we do have examples in the guidance. I would recommend not only looking at this particular guidance but, other digital health guidances that we have published.

And if it gives you an idea on such prediction tools or such risk categorization tools for certain user conditions, it may not necessarily meet one answer fits all. Because it depends on what disease, what condition, when it's used, etcetera.

So in short, I believe - you can reach out to us either through digitalhealth.fda.hhs.gov. Or write to DICE and we will be able to help you specifically, on your answers.

(Sema Palawel): Okay. Thank you.

Coordinator: Okay, thank you very much. Our next now is from (Peter Tow). Sir, your line is open.

(Peter Tow): Hello, thank you. Earlier in the presentation there was a slide that said, the Cures Act provides that a software function will not be excluded from the device definition if it is used in the manufacture and transfusion of blood and blood components.

Does that mean if a clinical decision support software is meant to provide guidance specifically on blood transfusions, that it would fall automatically, into device definition? And that the FDA would take a stronger regulatory stance on it?

Matthew Diamond: Essentially. Yes, it means that if it's intended for a purpose related to blood transfusions, it would not be excluded from the device definition, as you mentioned.

Bakul Patel: I just want to add to what Matthew said. However, I think that's the one criteria whether it's a device or not a device. And is regulated by Center for Blood Biologics or not.

I think the Center for Biologics that handle blood and blood transfusion software may have policies and may have approaches that may not necessarily

mean a one size fits all, for all the different types of risks. It's about the risks of that particular solution that matters.

So I would encourage you to reach out to that group to talk in detail about a very specific example that you may have.

Woman: And would that be the case even if the software still maintained the autonomy or independence of the physician's decision?

Bakul Patel: If it's specific to blood - blood and blood products, I would defer you to the Blood Establishment Group. And they use that for - I can speak for Center for Devices. And I can tell you that we do take the product risks into consideration, even after it's considered a device.

So the triage is, do you meet the definition of device or not? You're regulated by FDA. But the way we regulate products, once it's a device, is of course risk based. And not everything falls into one big category.

(Peter Tow): Thank you.

Coordinator: Thank you. Our next request now from (Eshay Sangacul). Your line is open sir. Thank you.

(Eshay Sangacul): Thank you. Thank you Bakul and Matthew. My question is, can you expand upon any interactions that you may have had with like CDER or CBER, concerning how Clinical Decision Support Software is used within clinical trials for drugs or biologics? Thank you.

Bakul Patel: We normally have I mean, various ongoing conversations on those topics. Especially as folks and trials and studies are incorporating a lot of these technologies.

So yes, I mean other than, this particular guidance is really more about, you know, how FDA would look like. Or help to (unintelligible) that are now either not a device or would continue to be devices, based on this Act that we are interpreting here.

So the short answer is yes, we have been talking to other centers and trying to align on our approaches as we move forward.

(Eshay Sangacul): Great. Thank you.

Coordinator: To ask a question, please press star then 1. Unmute your phone and record your name if you could. Our next now from (Mary Hahn). Ma'am, your line is open.

(Mary Hahn): Hi. Thanks for the opportunity. Following up on the - or the question earlier on drive clinical management, was hoping that you could comment further on how the agency is going to interpret, informed clinical management?

The guidance indicates that it is not intended to trigger an immediate or near-term action. But you could see a situation where a CDS - or a CDS function provides options for treatment. But in providing those options, within the context of a single encounter, may actually you know, trigger the healthcare provider to do something.

And so, trying to get a little bit of a better sense of how you would interpret the scope of what informed clinical management would cover.

Bakul Patel: Yes, so there's a larger document that was published by IMDRF which dives very specifically into the framework itself. That's harmonized and converged in thinking with all regulators. So I don't know if you have access to that guidance or not. It is on IMDRF.org - Software as a Medical Device section.

I would encourage you to take a look at that. I would say yes, there is this nuance about when an information is considered a recommendation and not a direction towards driving clinical management. I think that's the distinction we are drawing the guidance as well as, Cures talks about low risk products.

There are, under the control of a healthcare provider, and the provider has enough information to use the recommendations in a way that they're not necessarily only for diagnosing and treating. But actually take that into consideration for other aspects.

And our alignment to the IMDRF framework is exactly to align those two intentions and be clear. I believe like one other previous caller talked about, you know, is there going to be further clarity. And I believe we are getting a bunch of requests. And we will take that into consideration as we draft and think about how - where the confusion is and, where we need to provide more clarity.

Coordinator: Thank you. Our next question now from (Alex Freedman). Your line is open.

(Alex Freedman): Hi. Thank you very much for the presentation today and the very thoughtful update to the draft guidance.

So this is a follow-up to an earlier question regarding, how does a patient independently review information? So I hope maybe this could be a comment

as well. If you find it useful, then I'm happy to work within my organization to provide a comment.

I see it in two extremes I think, to consider. If a manufacturer generates a questionnaire, and it doesn't add that much value to the patient, then the manufacturer is probably not going to do it. So if the patient can very quickly, independently review all the information, then you haven't really helped the patient that much.

And then as you move forward, you know, and I said, extreme but, really take a moderate case. If you move forward and you organize information for that patient, whereby perhaps you're saving them time or educating them, I think I would accept that they can still independently review all the information.

And as Bakul said, that it's - that the manufacturer is fully transparent. That all this information is meant to educate, save you time, etcetera. I think that would fit into an example of a patient being independently able to review something.

So could you comment on that? If it's educate, save time, organize a publicly available information, is that a good description of independently reviewing things from a patient perspective?

Bakul Patel: Yes, and thank you for that, actually. That's really helpful in clarifying the previous caller's question. And you hit upon something. And we will take you up on the offer of supporting comments in your organization.

But you basically repeated what Matthew, in his presentation, highlighted when - in the box on IMDRF it says, aggregating information for options. Or

aggregating information - relevant information for that particular clinical situation.

So we would consider that to fit into the informed clinical management bucket where one can make enough - can provide enough information for a user to say, I'm going to take that or, I'm going to leave it. I think that's exactly the intent of this conversation.

(Alex Freedman): Okay, thank you very much. That's helpful.

Coordinator: And again, to ask a question, please press star then 1 and record your name. My last question at this time from (Paul Hammering). And sir, your line is open.

(Paul Hammering): Hi. Thank you. Yes, my question is, is whether these regulations are applicable to internally developed and applied technologies or software, or only commercially available?

Bakul Patel: So, in order to understand where FDA regulations apply, I think I would point you to the Mobile Medical Apps Guidance where - I'm presuming when you say internally, you're talking about a group practice or within a practice itself. And I'm assuming you're a healthcare provider.

If that's the case, there is a clear distinction where the healthcare provider in their patient provider relationship, can perform some of these functions to make things easier. Make things more efficient, etcetera.

However, when it's commercially distributed and marketed, for our general use, it's when - that's when the regulations sort of apply.

(Paul Hammering): Thank you.

Coordinator: Our next question, (Eddie Vahan Burgess), your line is open, sir.

(Eddie Vahan Burgess): Hi. It is related to the Criterion 4, and determining whether or the CDS, when the user is a (unintelligible), what does it mean that an input data is explained and available? If you can give an example it would be great.

Bakul Patel: I think it's - so what we are trying to explain here is, folks who are using or sharing what the logic and the rationale is in the - through the end user. I think it's important to - at least the proposal we put out in the draft guidance, it's important tell people, what went into making the recommendation. And that's really what we intend by that input.

(Eddie Vahan Burgess): So an explanation of what goes in, rather than detailing of the underlying value for each variable. I think you're guiding towards explanation rather than reporting of every information or the value that went in for individual patients. Is that correct?

Bakul Patel: Right. So, if I were to read the under criteria for, there's a fourth bullet in one of the slides which talks about underlying data used to develop the algorithm, plain language description of logic and rationale. And sources supporting the recommendation and basis of the recommendation, that's really what we're (unintelligible) to.

So the answer is yes. We want the users to understand. And the basis, as opposed to the mechanics.

(Eddie Vahan Burgess): Thank you very much.

Coordinator: Now our next question from (Mary Hahn). Your line is open, ma'am.

(Mary Hahn): Hi. Yes, another question building off of a previous question about, configurability and customization of tools. I'm hoping that you can provide a little bit more information about the agency's view of CDS tools that are provided for use by healthcare organizations whose content can be populated and configured by the healthcare organization.

And then again, the level of transparency is again controlled by the healthcare organization itself.

Bakul Patel: Yes, so I think you're talking - maybe I can take your question and make it generic. I think if you think about order sets and/or similar to order sets, clinical practice guidelines implemented in software. And if we were to think about it from that angle, what we have said as an agency is, a clinical practice guidelines implemented, and let known to users that's what they have done, that would continue to be in the way that the clinical (unintelligible) frames this conversation. As that's not something that would be under FDA's view.

Now I can imagine the scenario you are painting is across the spectrum. And I'm sure there's a case where an extremely easy, you know A plus B equals C, is a rule that has been created by a healthcare facility, now implements it and it can be made very transparent.

But I can also imagine a very complex, non-explainable situation can be considered as well. So I think when there's a situation like that, we encourage you to engage with us, number one.

But before you do that, I would recommend, both specific examples are exactly the kind of input we want in this comment period, that we're looking to get input from.

So your suggestions, your ideas, or your solutions for those situations or examples that would fit or that won't fit into this framework, would be really, really appreciated.

(Mary Hahn): Okay, thank you.

Coordinator: Thank you. And, our last question today is from (Isabel Puray). Ma'am your line is open.

(Isabel Puray): Yes. Hi, thanks for the great presentation. I just have a specific question for devices that are both intended for healthcare professionals and also patients, caregivers.

And for a case where for example, the FDA intends to regulate and have an oversight focus, for the patient part of the device but, not for the healthcare professional part, what would be expected in the pre-market submission? Because both users and intended users are listed in the product (unintelligible).

So my guess would be that the pre-market submission should cover all the uses of the product. And could you confirm if that would be correct?

Bakul Patel: Yes, so it's all about the intended use, right. So if the intended use and where it's going to be used, any pre-market submission, just like any other product we would want, the review process would need to know what your intention is.

And I think if your intention of the use of the product is broad, then we would expect that to be included in the submission.

(Isabel Puray): Okay, thank you.

Coordinator: Thank you for your questions. And now I'd like to turn the call back over to your host, Irene Aihie, for any closing remarks.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH Learn Web page at www.fda.gov/training/cdrhlearn by Tuesday, November 12.

If you have additional questions about today's presentation, please use the contact information provided at the end of the slide presentation. As always, we appreciate your feedback. Following the conclusion of today's Webinar, please complete a short 13 question survey about your FDA CDRH Webinar experience. The survey can be found at www.fda.gov/cdrhwebinar, immediately following the conclusion of today's live Webinar. Again, thank you for participating. This concludes today's Webinar.

Coordinator: And again, as today's event is concluded, thank you for your participation. Please go ahead and disconnect at this time. Thank you very much.

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