



## *Weighing the Impact of FDA Regulatory Uncertainty on Clinical Decision Support Development*

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### **Executive Summary**

Clinical decision support (“CDS”) software is not getting the regulatory clarity it needs and deserves. Although the United States Food & Drug Administration (“FDA”) made CDS software guidance an “A-list” priority in its 2015 regulatory agenda, the Agency has yet to define the portion of CDS software it intends to regulate and, for that portion it does regulate, the appropriate regulatory pathway to market.

Of course, developing a regulatory framework for CDS software is no easy task, as FDA must strike a delicate balance between ensuring patient safety and promoting innovation. However, until a regulatory approach is defined, CDS innovators will be left in the dark with regard to the expected costs and timelines for CDS development. Such uncertainty has already contributed to delays in CDS products reaching the market and, worse yet, the abandonment of CDS development projects altogether.

In fact, in a recent survey of CDS developers, nearly two thirds reported encountering delays due to regulatory uncertainty, and one third reported that regulatory uncertainty caused them to abandon development of a CDS product. Without clear regulatory guidance on which CDS products will be regulated and, for those that are, how such products will be regulated, valuable CDS tools, which can improve health outcomes, enhance the quality and consistency of care, and increase efficiency, will be kept out of the hands of clinicians and patients.

### **Introduction**

Clinical decision support (“CDS”) software, which analyzes clinical and nonclinical data to guide health care decision-making, has the potential to drive significant improvements in health care quality and efficiency. However, today’s CDS developers face a key impediment to product innovation: a largely uncertain regulatory climate at the United States Food & Drug Administration (“FDA”). Even though FDA is aware of this issue, and is reportedly developing guidance regarding these products, at present, there is no definitive regulatory framework to inform innovators’ CDS development strategies. This uncertainty has caused concerning delays in CDS development, and has even forced some firms to abandon development projects altogether.

To get a better sense of the real-world impact that regulatory uncertainty is having on CDS development, the CDS Coalition, a group focused on ensuring a clear, risk-based regulatory framework for CDS software that appropriately balances the need for regulatory oversight with

the need for innovation,<sup>1</sup> recently conducted an online survey of CDS developers.<sup>2</sup> The survey was completed by 48 respondents, representing a wide range of organizations with regard to both size and experience levels. For an industry estimated to be in the magnitude of a couple hundred firms, the sample size nicely represents a cross-section of that industry.

This white paper will weave the results of the survey into a discussion of: (1) the current landscape of CDS developers; (2) the potential benefits of CDS software, illustrated by three specific examples, as well as the potential risks; (3) legislative and FDA action in defining a regulatory approach to CDS software; and (4) the effects of regulatory ambiguity on CDS software development.

## **I. Defining the Landscape**

CDS developers generally are a sophisticated group, in many cases with years of health care and CDS-specific experience.

The 48 survey respondents cover the full range of company sizes as well as level of industry experience. Indeed, the respondents included in almost equal measure the two main types of industry participants: startup companies (40%), and large cap companies (33%). In line with this breakdown, 38% reported having 1-10 employees, while another 38% reported having 700+ employees. With the large number of start-up company respondents, it is unsurprising that nearly 45% reported being in business for five years or less. Yet, half reported that they have been operating for over 10 years.

Survey results also suggest that CDS developers are quite sophisticated in their health care experience. Nearly 80% of respondents reported that more than 90% of their company's business is devoted to the health care space. In addition, nearly 30% reported being involved in CDS development for over five years. This indicates that CDS developers are not just tech companies experimenting in health care, but serious health care companies with true expertise in the space.

CDS developers generally recognize the clinical and technological complexity of their work. Nearly all respondents (39 of 41 who answered this question) reported that they engage clinicians and/or scientists to assist in the product development process.<sup>3</sup> However, CDS developers do much more than engage expert consultants.

Developers also reported pursuing various types of premarket and postmarket studies to validate their products, including the gold-standard, randomized controlled trials ("RCTs"). On a premarket basis, health care professional usability testing, patient usability testing and case reports were the most popular types of studies performed by developers. Significantly, however,

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<sup>1</sup> The CDS Coalition is comprised of software providers, IT infrastructure manufacturers, health care providers, medical device and pharmaceutical manufacturers, trade groups and members of the clinical community.

<sup>2</sup> The survey took place during December 2015 to January 2016.

<sup>3</sup> Physicians were the most common type of clinician engaged by companies (with 35 of 41 respondents indicating they worked with physicians).

15% (6 of 39 respondents) stated that they performed or planned to perform premarket RCTs. On the postmarket side, usability testing and market research were the most popular study types among CDS developers.

CDS innovators are clearly devoting substantial time, resources and clinical and tech-focused brainpower to product development activities, and for good reason – CDS software holds great potential for improving the public health.

## **II. The Need for a Regulatory Approach that Balances Value and Risk**

From improving treatment adherence to enhancing medical education and training, CDS software can provide numerous benefits. Among survey respondents, improved patient outcomes and increased health care quality were among the top anticipated benefits of developers' products. A deeper dive into three specific examples of CDS software further illuminates the value of these products. We have made these anonymous, but they are reflective of common examples.

First, consider “Engage,” a CDS tool that utilizes patient data to generate actionable clinical recommendations at the point of care. Engage, which is currently used in the cardiology space, helps ensure that patients receive the right care at the right time by assisting physicians in recognizing conditions (with a particular focus on identifying high risk conditions). Engage is integrated into the provider's electronic medical record (EMR) system to provide a seamless user experience. The tool can prevent medical emergencies, as well as costly and time-consuming tests and procedures.

Another CDS product is “DiagnosisHelper,” a web-based diagnosis checklist tool. Using patient demographics as well as clinical features (e.g., “pain radiating to back” or “persistent cough”), DiagnosisHelper returns a list of potential diagnoses, including time-sensitive “Don't Miss Diagnoses.” DiagnosisHelper also provides access to knowledge from medical textbooks, journals, and internal guidelines and protocols regarding the potential diagnoses. The tool can be used on its own or can be integrated into a provider's EMR system. The improvements in diagnosis quality resulting from the use of DiagnosisHelper can lead to more appropriate referrals and testing, and reduced clinical risk, among other benefits.

A third CDS product is “DrugAid,” a platform for performing medication reviews to reduce medication risks. DrugAid considers the entire risk landscape of patients' medications and supplements and models additive side effects, drug interactions, contraindications and precautions of a patient's “before” regimen versus the patient's “after” regimen. Clinicians can also use the DrugAid to search for replacement medications and determine how the risks would be different by using that replacement medication.

While the three CDS products described above are tools designed to assist clinicians (and most survey respondents reported that the primary intended user group for their CDS product(s) was physicians),<sup>4</sup> some CDS products are being designed for direct patient use (and benefit).

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<sup>4</sup> Other reported intended user groups included nurses and caregivers.

The intended user group is an important factor to consider in the overall risk equation for CDS products.

CDS products carry varying levels of risk. On the lowest end of the risk spectrum are products such as a body mass index calculator or a medication reminder where users are clearly not dependent on the CDS software in making their health care decisions. However, as the user's dependence on the CDS software to make health care decisions increases, the risk associated with the software also increases. Based on this framework, a low to medium risk CDS product may be software for clinician use that predicts drug-drug interactions. A medium to high risk CDS product may be software intended for patients (i.e., untrained users) to assess complex cardiovascular health risk factors. Finally, CDS products that would likely fall into the high risk category include radiation dose calculators and software that assists clinicians in providing recommendations for cancer treatment. However, this "dependence" standard is not the only possible method of categorizing the risk of CDS software.

According to the International Medical Device Regulators Forum (IMDRF's) Software as Medical Device (SaMD) Working Group, CDS software can be broken down into four different categories based on (1) the significance of the information provided by the software to the health care decision and (2) the state of health care situation or condition the software is intended to address.<sup>5</sup> These categories can help classify the risk of a given CDS product.

With respect to the first criterion, the largest group of respondents (48%) stated that their product was intended to "drive clinical management of a disease or condition," 35% stated it was to "inform clinical management" and 18% said it was to "treat or diagnose a disease or condition (all out of 40 total respondents).<sup>6</sup> There was a similar spread of responses regarding the second criterion, with "serious situation or condition" taking the lead (48%), followed by "non-serious situation or condition" (33%) and then "critical situation or condition" (20%) (all out of 40 total respondents).<sup>7</sup>

In light of these particular responses, as well as other survey responses generally, it appears that many of the respondents are involved in developing higher risk CDS products. This is unsurprising as developers with CDS products on the lower end of the risk spectrum are bound to be less concerned with FDA regulation of their products (perhaps because some do not expect to be subject to regulation at all), and therefore less likely to complete our survey. It is those developers with higher risk CDS products who have the greatest stake in pressing FDA to establish a regulatory framework that appropriately balances the value of clinician and patient access CDS software with ensuring patient safety. It is that group, we believe, that completed the online survey.

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<sup>5</sup> IMDRF SaMD Working Group, "*Software as a Medical Device*": Possible Framework for Risk Categorization and Corresponding Considerations (Sept. 18, 2014), <http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf>.

<sup>6</sup> See IMDRF document above for category definitions.

<sup>7</sup> See IMDRF document above for category definitions.

It is also important to understand that in many ways risk and benefit go hand-in-hand. CDS products might be higher risk precisely because they deal with more serious disease in a more significant way. And that makes the results of the survey all the more disturbing because it is these higher benefit software products that are being stymied by the lack of regulatory clarity.

### **III. Legislative and Regulatory Efforts Surrounding CDS**

As noted previously, to date, FDA has not established a system for discerning regulated from unregulated CDS, nor has it provided a pathway for regulating the higher risk portion of CDS. However, legislation has been introduced that would clarify FDA's approach to these products. Congress is considering the Medical Electronic Data Technology Enhancement for Consumers' Health ("MEDTECH") Act (S. 1101), sponsored by Senators Orrin Hatch (R-Utah) and Michael Bennet (D-Colo.) to define which CDS products are subject to regulation. Specifically, the Act makes a distinction between CDS software that analyzes data to simply assist a clinician versus software on which a clinician is dependent to make a patient care decision. The legislation is slated to be discussed as a part of a March 9, 2016 executive session of the Senate Health committee in regard to the committee's biomedical innovation bills.

On the regulatory side, FDA has been discussing development of CDS guidance since 2011.<sup>8</sup> Developing draft CDS guidance was even slated as an "A-list" priority on FDA's regulatory agenda in 2015.<sup>9</sup> However, it is now early 2016, and CDS stakeholders are still waiting. In the absence of such guidance, nearly 65% of survey respondents<sup>10</sup> agreed that FDA has not provided clarity with respect to the CDS products it will regulate. Without clear rules, innovators are left in a gray area, unsure if their CDS software is subject to regulation (and if so, the nature of that regulation). Given that FDA regulation carries with it substantial impact on both cost and time frames, that sort of uncertainty negatively impacts product development.

### **IV. The Effects of Regulatory Uncertainty on CDS Development**

Despite regulatory uncertainty, some innovators are trying to move ahead with CDS development. Unfortunately, their path forward has not been an easy one. Like nearly any product development, CDS development requires adequate funding. Investors, though, typically ask for a business plan that includes an accurate estimate of costs as well as time-to-market. Unfortunately, in the current environment, innovators in this space simply cannot give investors accurate estimates of either cost or timing.

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<sup>8</sup> FDA, *Public Workshop - Mobile Medical Applications Draft Guidance* (Sept. 13, 2011), <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm275909.htm>.

<sup>9</sup> FDA, *CDRH Fiscal Year 2015 (FY 2015) Proposed Guidance Development and Focused Retrospective Review of Final Guidance*, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAlII/ucm321367.htm>.

<sup>10</sup> Thirty-nine respondents answered this question.

As a result, thirty-six percent of survey respondents<sup>11</sup> reported that not knowing whether FDA will regulate their CDS product has made it difficult for them to secure funding for product development. Likewise, 36%<sup>12</sup> of those who know their software is FDA regulated reported that not knowing the FDA-required steps to develop their CDS product has made it difficult for them to secure funding. Investors (whether they are angel investors, venture capitalists or company management) are simply hesitant to invest in CDS products when the burden (in terms of both time and cost) of FDA regulation is uncertain.

More than just having trouble finding money, the uncertainty itself produces delays. Sixty-two percent of survey respondents<sup>13</sup> reported that they have encountered a delay in the development of a CDS product due to regulatory uncertainty. While most respondents reported delays lasting between one month and one year, 20% experienced delays lasting more than one year. What is more troubling than delays, however, is that one third reported that they have had to abandon altogether the development of a CDS product due to regulatory uncertainty. Simply put, FDA's lack of a regulatory framework for CDS software is stifling innovation and keeping valuable new products from reaching the market.

## **Conclusion**

Prompt legislative and/or regulatory action is needed to clarify the scope of CDS software that will be subject to FDA regulation as well as the specific regulatory requirements that will apply to any software that is regulated. Until the regulatory playing field for CDS software is better defined, it is likely that powerful and potentially life-saving CDS tools will be kept out of clinicians' and patients' hands.

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<sup>11</sup> Forty respondents answered this question.

<sup>12</sup> Forty respondents answered this question.

<sup>13</sup> Thirty-nine respondents answered this question.