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CITIZEN PETITION

February 6, 2023

Epstein Becker & Green, P.C. through the undersigned submits this Petition under 21 C.F.R. § 10.25(a) and § 10.30 to the U.S. Food and Drug Administration ("FDA" or "the agency") on behalf of the Clinical Decision Support Coalition ("CDS Coalition", "Coalition" or "Petitioner") to request the Commissioner of Food and Drugs to rescind the Final Guidance on Clinical Decision Support Software on September 28, 2022 (the "CDS Guidance"), which violates the Federal Food, Drug, & Cosmetic Act (the "FD&C Act"), and repropose the CDS Guidance to follow the statutory language of subsection (o) of the 21st Century Cures Act (the "Cures Act").

By way of background, the CDS Coalition is a diverse and balanced group of stakeholders such as clinical decision support software developers that have been traditionally unregulated, IT infrastructure manufacturers, and regulated medical device manufacturers, all of whom have a stake in drawing the correct jurisdictional line between regulated and unregulated software. The Coalition's goal is to ensure a risk-based and clearly defined regulatory system for clinical decision support ("CDS") software that appropriately balances the need for regulatory oversight with the need for innovation and access to new technology.

## A. Action Requested

Petitioner requests that the Commissioner rescind the final CDS Guidance and repropose the guidance to follow the statutory language of subsection (o) of the Cures Act. Among other things, in the reproposed guidance FDA should clarify that CDS software can indeed recommend a single diagnosis or single treatment pathway, and that the time critical nature of the decision-making is not a bar under Criterion 3 of the Cures Act requirements for CDS (intended for the purpose of "supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition"), but rather a factor to be considered under Criterion 4 of the Cures Act (intended for the purpose of "enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient").

## B. Statement of Grounds

## 1. EXECUTIVE SUMMARY

Here are a few of the Coalition's major points that will be discussed further in this Petition:

- The Office of the National Coordinator for Health Information Technology ("ONC") and the Centers for Medicare and Medicaid Services ("CMS") strongly believe that CDS software will help improve the quality of care, and that innovation must be encouraged in this space. Congress laid bare those same intentions and intentionally carved out certain CDS functionality from FDA regulation as a medical device under the Cures Act. FDA's action in publishing the CDS Guidance is at odds with these other federal policies and congressional intent.
- FDA's own record in connection with CDS software shows that there is no public health problem to be solved.
- FDA is harming, not helping, public health by dissuading innovators from evolving CDS software for the betterment of the public and imposing arbitrary rules on technology development that do not serve their intended purpose.
- FDA is doing an end run around the process that Congress set up for the agency to expand its regulatory oversight in the event the agency identified a problem requiring it to do so. Since there isn't a problem to be solved, FDA has no reasonable basis to support its position were it to use this statutory process, so it appears to be trying to evade the process by publishing a guidance document instead.
- FDA is improperly intruding into U.S. state jurisdiction over the practice of medicine and thus violating the Constitution.
- FDA violated the FD&C Act by publishing the CDS Guidance without an adequate notice that gave the public a legitimate opportunity to comment.
- FDA violated the FD&C Act by disregarding the plain language of the statute, and instead inventing its own interpretation that flies in the face of congressional intent.
- FDA is taking on regulatory responsibilities that are not sustainable.
- In doing all of this, FDA is compromising its own ability to enforce the law under its purview and setting a bad example for the public, flagrantly thumbing its nose at the law to which it is subject.

Petitioner requests that the FDA Commissioner rescind the final CDS Guidance and repropose the guidance to align with the statutory language, as explained more below.

## 2. INTRODUCTION: HISTORY OF THE DEVELOPMENT OF THE CDS GUIDANCE AND THE ROLE OF THE CDS COALITION IN THAT PROCESS

The Coalition was formed in early 2012, more than 10 years ago, soon after FDA announced in September 2011 at a public workshop that the agency was going to develop a guidance document on CDS. The Coalition participated in the Food and Drug Administration Safety Innovation Act ("FDASIA") Working Group (through the undersigned Co-chairing the Regulatory Subcommittee) that first addressed the policy and regulatory issues around defining the scope of

FDA regulation regarding CDS software.[1] FDASIA, in turn, was established at Congress' request and required the FDA, ONC and Federal Communications Commission ("FCC") to collaborate and to report to Congress "a proposed strategy and recommendations on an appropriate, risk-based regulatory framework pertaining to health information technology, including mobile medical applications, that promotes innovation, protects patient safety, and avoids regulatory duplication."[2] The FDASIA Health IT Report (the "FDASIA Report") that resulted specifically addressed the issues related to CDS software.[3] One of the issues motivating Congress to create FDASIA was a desire to have better informed policy making about where software was a device versus where it was clinical decision support. In particular, there was a desire to clearly draw that line so that companies developing software health care products and services could better plan for the appropriate set of regulations. The FDASIA Report was sent to Congress in April 2014.

Throughout the years 2012 through 2015, the Coalition met with FDA to contribute to the CDS policy discussion. In those discussions, the Coalition urged FDA to exclude software that was suitably transparent. The rationale for that policy approach was the need to articulate the dividing line between FDA jurisdiction and the practice of medicine overseen by state boards of medicine. If the software was transparent such that the users could reach their own conclusions without reliance on the software, any error the users make is properly within the jurisdiction of the state regulators overseeing the practice of medicine.

Given that FDA did not accept that policy recommendation, the Coalition then changed its focus to a legislative one by discussing the issue with Congress, as Congress had expressed interest in these issues dating back to 2012. Congressional leaders engaged in discussions with both the Coalition and FDA, going back and forth between the groups to make sure they (the members of Congress) understood the issues. After hearing both sides, out of respect for the state regulators and the Constitution, members of Congress wrote section 3060 of the Cures Act that added a new subsection 520(o)(1)(E) to the Act defining the FDA scope of regulation regarding CDS software. Certain CDS software functions are excluded from the definition of device by that section if the software functions meet the following four criteria:

> (1) not 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;[4]
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> (2) intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);[5]

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[1] 79 Fed. Reg. 19100 (April 4, 2014).

[2] P.L. 112-114, § 618 (2012).

[3] FDASIA Health IT Report, ONC, at 26–27 (April 2014), at, https://www.healthit.gov/sites/default/files/fdasiahealthitreport_final.pdf (hereinafter the "FDASIA Report").

[4] *See* FD&C Act § 520(o)(1)(E); 21 USC § 360j(o)(1)(E).

[5] *See* FD&C Act § 520(o)(1)(E)(i); 21 USC § 360j(o)(1)(E)(i).

> (3) intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition;[6] and
>
> (4) intended for the purpose of enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.[7]

It was thought that congressional enactment of subsection (o) drew clear lines between software that the FDA should evaluate as a device and that which it should not. Indeed, after the new statutory language was enacted, FDA proposed two interpretations via draft guidance, the first in 2017 and the second in 2019. With respect to the 2019 draft, FDA stated that its intent was to create a framework that will "prioritize patient safety while also recognizing that overregulation could stifle advancements in medical software and clinical support."[8] While both versions had their flaws, neither version contained the structural defects that surfaced for the first time in the 2022 CDS Guidance (including, for example, the addition of new content such as the concept of "automation bias", as discussed further below). The CDS Guidance as drafted now effectively undoes Congress's efforts to promote clarity and permits the FDA to regulate conduct that Congress has long held is properly overseen by the states.

The job of any administrative agency is to follow the law, not ignore or circumvent it. This Petition is rather simple: we are asking FDA to rescind the CDS Guidance and propose a revised guidance addressing the issues that we raise in this Petition.

## 3. WHAT IS CDS AND WHY FDA SHOULD ENCOURAGE IT

As the ONC, which is congressionally directed to develop recommendations relative to software, explains, CDS "provides clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care. CDS encompasses a variety of tools to enhance decision-making in the clinical workflow. These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information, among other tools."[9]

CDS "can significantly impact improvements in quality, safety, efficiency, and effectiveness of health care. [ONC] supports efforts to develop, adopt, implement, and evaluate the use of CDS to

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[6] *See* FD&C Act § 520(o)(1)(E)(ii); 21 USC § 360j(o)(1)(E)(ii).

[7] *See* FD&C Act § 520(o)(1)(E)(iii); 21 USC § 360j(o)(1)(E)(iii).

[8] FDA Statement, Statement on new steps to advance digital health policies that encourage innovation and enable efficient and modern regulatory oversight (Sept. 26, 2019).

[9] Clinical Decision Support, HealthIT.gov (last updated April 10, 2018), at https://www.healthit.gov/topic/safety/clinical-decision-support.

improve health care decision making."[10] More specifically, ONC explains "CDS has a number of important benefits, including:

1. Increased quality of care and enhanced health outcomes
2. Avoidance of errors and adverse events
3. Improved efficiency, cost-benefit, and provider and patient satisfaction"[11]

How does CDS do that? Among other things, CDS helps doctors avoid mental mistakes by expanding their thinking, reminding them of things they may know but have forgotten or otherwise missed. Further, as IBM has pointed out, just in oncology, "[i]n 2015, nearly 44,000 oncology research papers were published in medical journals around the world, or more than 120 new papers each day, outpacing the ability of humans to keep up with the proliferation of medical knowledge."[12] CDS helps doctors stay current in the face of an avalanche of new medical information. And, finally, there is an equal proliferation of published best practices in clinical guidelines that major health care institutions study through their committees, often their pharmacy and therapeutics, or P&T, committee. Once the hard work of wading through all the research is done, the committees need a mechanism to communicate those best practices to their medical staff. For this, they often turn to CDS.

In 2020, a group of researchers published an "An overview of clinical decision support systems: benefits, risks, and strategies for success" in Nature's online publication.[13] The article included a history of the development of CDS software starting in the 1970s, leading up to widespread adoption of sophisticated CDS. The authors observed that "in 2017, 40.2% of US hospitals had advanced CDS capability (HIMSS Stage 6)." This is all to say that CDS software is not new to the industry, such that the FDA CDS Guidance wouldn't really have an impact—in fact it is quite the opposite. CDS has become, quite simply, ubiquitous. The present market for such software is at about $4.5 billion.[14] These reasons are largely why other federal agencies are encouraging CDS software, and why FDA should follow suit.

## 4. FEDERAL POLICY SEEKS TO ENCOURAGE CDS AS PART OF MEANINGFUL USE OF EHRS, WHILE THE FDA CDS GUIDANCE DISCOURAGES CDS BY INCREASING REGULATORY BURDENS

The federal government has been using financial incentives to encourage the adoption of CDS since at least 2011. As part of its Electronic Health Records ("EHR") Incentive Program, CMS introduced the Clinical Decision Support requirement as a Stage 1 Eligible Professional

[10] *Id.*; *see also* FDASIA Report at 26.

[11] *Id.*

[12] The future of health is cognitive, IBM Healthcare and Life Sciences (June 2016), at https://www.ibm.com/downloads/cas/LQZ0O1WM.

[13] Sutton, R.T., Pincock, D., Baumgart, D.C. *et al.*, An overview of clinical decision support systems: benefits, risks, and strategies for success, npj Digital Medicine (Feb. 6, 2020), at https://www.nature.com/articles/s41746-020-0221-y#auth-Karen_I_-Kroeker.

[14] Clinical Decision Support Systems Market Size, Share & Trends Analysis Report By Product, Market Analysis Report, Grand View Research (2020), at https://www.grandviewresearch.com/industry-analysis/clinical-decision-support-system-market.

Meaningful Use Core Measure (Measure #10.[15] The Stage 2 Eligible Professional Meaningful Use Core Measures (Measure #6) also addresses CDS.[16] As explained by CMS, the goal is to get EHR users to "[u]se clinical decision support to improve performance on high-priority health conditions."[17] Introduced in 2012, the first measure that CMS used to assess whether there is meaningful use qualifying for reimbursement is for the user to "Implement five clinical decision support interventions related to four or more clinical quality measures at a relevant point in patient care for the entire EHR reporting period. Absent four clinical quality measures related to an EP's scope of practice or patient population, the clinical decision support interventions must be related to high-priority health conditions."[18]

The requirements have evolved to require more and more engagement with CDS.[19] The rule now defines CDS as "HIT functionality that builds upon the foundation of an EHR to provide persons involved in care processes with general and person-specific information, intelligently filtered and organized, at appropriate times, to enhance health and health care."[20] Indeed, the federal government has, since 1996, enacted a whole series of laws to improve the use of digital health information in clinical practice to improve care, reduce medical errors, etc.[21] Even CMS guidance is consistent with the long-standing congressional pursuit of using digital tools, and hence software, to support improved clinical outcomes; CMS makes it clear that such CDS includes specifically "diagnostic support."[22]

FDA's actions in publishing the CDS Guidance unnecessarily increase regulatory burden that discourages the very innovation that CMS and ONC are trying to encourage. For example, with

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[15] Eligible Professional Meaningful Use Core Measures, Measure 10 of 13, CMS (last updated May 2014), at https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/downloads/11_Clinical_Decision_Support_Rule.pdf.

[16] 45 CFR 170.314(a)(8) and (a)(2); *see also* Stage 2 Eligible Professional Meaningful Use Core Measures, Measure 6 of 17, CMS (Oct. 2012), at https://www.cms.gov/regulations-and-guidance/legislation/ehrincentiveprograms/downloads/stage2_epcore_6_clinicaldecisionsupport.pdf.

[17] Stage 2 Eligible Professional Meaningful Use Core Measures, Measure 6 of 17, CMS (Oct. 2012), at https://www.cms.gov/regulations-and-guidance/legislation/ehrincentiveprograms/downloads/stage2_epcore_6_clinicaldecisionsupport.pdf.

[18] 77 Fed. Reg. 53967, 53998 (Sept. 4, 2012); 42 CFR 495.22(e)(2)(ii)(A)(1).

[19] *See, e.g.,* Eligible Professional Meaningful Use Core Measures, Measure 10 of 13, CMS (last updated May 2014), at https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/downloads/11_Clinical_Decision_Support_Rule.pdf; Eligible Professional Medicaid EHR Incentive Program Stage 3 Objectives and Measures, Objective 3 of 8, CMS (Aug. 2017), at https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/Downloads/MedicaidEPStage3_Obj3.pdf.

[20] 75 Fed. Reg. 44313, 44350 (July 28, 2010); Clinical Decision Support: More Than Just 'Alerts' Tipsheet, eHealthUniversity, CMS (Sept. 2014), at https://www.cms.gov/regulations-and-guidance/legislation/EHRincentiveprograms/downloads/clinicaldecisionsupport_tipsheet-.pdf.

[21] Douville, S, editor, Advanced Health Technology: Managing Risk While Tackling Barriers to Rapid Acceleration 1st Edition, ch. 13. (2022).

[22] Clinical Decision Support: More Than Just 'Alerts' Tipsheet, eHealthUniversity, CMS (Sept. 2014), at https://www.cms.gov/regulations-and-guidance/legislation/EHRincentiveprograms/downloads/clinicaldecisionsupport_tipsheet-.pdf.

data science it is now possible to develop a comprehensive picture of the health history of a person who has been ill for a while, or who has complex, comorbid conditions, using data science, the digital claims data Congress required to be created in 1996, and the digital clinical data in EHRs that Congress paid for with the Meaningful Use program. Its very point in this twenty-year exercise was to ensure that we could use software to understand the health care system at a population level AND an individual's health as well.[23] With advances in computing, we can only expect more data-science driven innovation in health care, which is precisely what Congress sought, and sought to reinforce, with subsection (o) of the Cures Act. In this context, however, FDA's CDS Guidance, because it exceeds Congress's statutory definitions of what is considered CDS compared to a regulated medical device, threatens to undermine the very goal Congress sought.

## 5. UNREGULATED CDS IS SAFE

Congress, in its wisdom, at the same time it amended the FD&C Act to carve transparent software out of FDA regulation, required in section 3060(b) that FDA periodically conduct an investigation and report to Congress on any safety or effectiveness signals that it was picking up with regard to the unregulated software. Specifically, that section provides:

> (b) REPORTS.—The Secretary of Health and Human Services (referred to in this subsection as the ''Secretary''), after consultation with agencies and offices of the Department of Health and Human Services involved in health information technology, shall publish a report, not later than 2 years after the date of enactment of this Act and every 2 years thereafter, that—
> (1) includes input from outside experts, such as representatives of patients, consumers, health care providers, startup companies, health plans or other third-party payers, venture capital investors, information technology vendors, health information technology vendors, small businesses, purchasers, employers, and other stakeholders with relevant expertise, as determined by the Secretary;
> (2) examines information available to the Secretary on any risks and benefits to health associated with software functions described in section 520(o)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j) (as amended by subsection (a)); and
> (3) summarizes findings regarding the impact of such software functions on patient safety, including best practices to promote safety, education, and competency related to such functions.

FDA has done that in the years since the 2016 legislation, and filed reports with Congress in 2018, 2020 and 2022 that say unregulated CDS software is safe.[24]

In FDA's 2018 report to Congress, FDA adopted the definition it had proposed for CDS in the agency's 2017 draft CDS guidance. Note that in this report, FDA reviewed all five categories of

[23] Douville, et al, *supra* note 20.

[24] Digital Health Reports, FDA (last updated Dec. 8, 2022), at https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-reports?utm_medium=email&utm_source=govdelivery.

exempted software, including CDS. In each summary below, we provide the top line summary applicable to all five, and then the details around CDS. In the 2018 report to Congress, FDA concluded:

> The majority of findings detailed in this report correspond to positive impacts on patient safety and health benefits related to use of the five software functions. This report identifies only a few reported negative impacts on patient safety and health.
> . . .
> [Clinical Decision Support]
>
> Impact to Patient Safety
>
> Research identified an association between software types, such as those used to identify drug drug interaction (DDI)-induced adverse drug reactions (ADRs) and multi-step biomedical informatics screening, and outcomes that could positively impact patient safety. The literature suggests that information populated from these software functions can be used to select drug combinations that avoid potential ADRs, suggest alternatives that minimize the number of DDI induced ADRs, facilitate drug repurposing, and screen for drug combinations that either mitigate undesirable toxicity or synergize therapeutic effects. Implementation of other clinical decision support tools using a prospective pre- and post-intervention design showed a positive impact on standard of care guideline discussions during clinical care rounds. FDA received one adverse event related to a clinical decision support software function. The particular software bug led to a dosage calculator using the incorrect date of birth to calculate estimated values needed in a medication dosage computation, which could result in a patient receiving an incorrect dose.[25]

In 2018, there was simply no cause for alarm. FDA found no problems regarding CDS other than one adverse event report. This is consistent with the FDASIA Report, which stated that the focus should be not on function but on risk of harm.[26]

In the year 2020, FDA found the same thing. According to FDA, "In general, the analysis found more benefits than risks to patient safety and health related to these software functions."[27] Specifically with regard to CDS, the report discussed a few studies that had been published. It then went on to analyze adverse event reports:

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[25] Report on Non-Device Software Functions: Impact to Health and Best Practices, FDA (Dec. 2018), at https://www.fda.gov/media/119187/download (citations deleted).

[26] FDASIA Report at 27

[27] Report on Risks and Benefits to Health of Non-Device Software Functions, FDA (Nov. 2020), at https://www.fda.gov/media/143795/download.

> FDA received four adverse event reports where CDS software did not alert clinicians to potential risks when ordering medication. Two of these events involved CDS software not alerting clinicians to a medication order that prescribed duplicate or interacting medications. A third event involved CDS software not performing drug interaction checks when two medications received new codes. The reports did not cite any impacts to patients' safety resulting from these issues. A fourth event involved a CDS function within an EHR system not alerting clinicians to a patient's allergy when prescribing medication. Clinicians administered a medication that conflicted with the patient's allergy and the patient went into anaphylaxis. The patient was in critical condition and required an airlift to a larger hospital for further treatment.

A total of four adverse event reports associated with what was, at that point, a multibillion dollar industry. And, again, the conclusion of the agency was that there were more benefits than risks associated with CDS.

Finally, just recently, FDA came out at the end of 2022 with its third report. In this report, the agency concludes, "In general, the analysis found more benefits than risks to patient safety and health related to these software functions."[28] In assessing the impacts to health, the agency observed that, "Numerous studies examined whether incorporating CDS software into EHRs improved adherence to guideline-based treatment for various conditions."[29] After discussing the specific studies, FDA made no indication in the report that there were any adverse events reported.

So again, just months ago, the agency concluded that the benefits of CDS software outweigh the risks.

Why go through each of these reports in this Petition? It is to highlight two takeaways that are the bases of this Petition:

> First, FDA lacks the factual basis to argue that there is a public health problem to be solved through its new CDS Guidance. To those who would justify FDA's actions by arguing that it was necessary to protect the public health, FDA's own investigations simply do not support that.
>
> Second, FDA took a shortcut of simply changing a regulatory guidance document because it knew that it couldn't justify a more formal action to enlarge its regulation of CDS.

What more formal action are we referring to? Congress, again in its wisdom but also likely at the request of FDA, specifically added to section 520(o) of the FD&C Act the following subsection to address the instances where FDA finds that the statutory exemption is too broad and is allowing

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[28] Report on Risks and Benefits to Health of Non-Device Software Functions, FDA (Dec. 2022), at https://www.fda.gov/media/163762/download.

[29] *Id*.

unsafe products to the market. The reference in the first paragraph to subparagraph (E) is a reference to CDS software.

> "(3)(A) Notwithstanding paragraph (1), a software function described in subparagraph (C), (D), or (E) of paragraph (1) shall not be excluded from the definition of device under section 201(h) if—
>
> (i) the Secretary makes a finding that use of such software function would be reasonably likely to have serious adverse health consequences; and
>
> (ii) the software function has been identified in a final order issued by the Secretary under subparagraph (B).
>
> (B) Subparagraph (A) shall apply only if the Secretary—
>
> (i) publishes a notification and proposed order in the Federal Register;
>
> (ii) includes in such notification the Secretary's finding, including the rationale and identification of the evidence on which such finding was based, as described in subparagraph (A)(i); and
>
> (iii) provides for a period of not less than 30 calendar days for public comment before issuing a final order or withdrawing such proposed order.
>
> (C) In making a finding under subparagraph (A)(i) with respect to a software function, the Secretary shall consider—
>
> (i) the likelihood and severity of patient harm if the software function were to not perform as intended;
>
> (ii) the extent to which the software function is intended to support the clinical judgment of a health care professional;
>
> (iii) whether there is a reasonable opportunity for a health care professional to review the basis of the information or treatment recommendation provided by the software function; and
>
> (iv) the intended user and user environment, such as whether a health care professional will use a software function of a type described in subparagraph (E) of paragraph (1).

Thus, Congress expressly gave FDA the power to enlarge its regulatory oversight if the facts support it doing so. All the agency has to do is go through the notice and comment process and share the data of concern, allowing for public comment on that data.

But the FDA didn't do so for CDS. The agency failed to follow the specific provision Congress had put in place to address any concerns FDA might have about unsafe products being inappropriately exempted. Nor could the FDA satisfy that requirement if it had tried—its own records show that there is no problem to be solved related to CDS. CDS software is not causing any substantial harm, but is instead delivering significant benefits to patients.

## 6. STATES COMPREHENSIVELY REGULATE THE PRACTICE OF MEDICINE

### *a. State Boards of Medicine*

FDA is treading on a Constitutional right in its CDS Guidance by attempting to regulate the practice of medicine, infringing upon the role of the states to ensure the health and safety of their citizens. According to the Federation of State Medical Boards or FSMB:

> Unlike many countries with centralized or national oversight of medical practice, the United States uses a state-based system for medical regulation. This is not by accident.
>
> The 10th Amendment of the United States Constitution authorizes the states to establish laws and regulations protecting the health, safety and general welfare of their citizens.
>
> Thus, it is the responsibility of the individual states to regulate the practice of medicine.
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> . . .
>
> The boards are a vital part of our health care system and do a remarkably effective job in keeping patients safe and ensuring quality in medical care.[30]

FSMB explains how the boards oversee errors by physicians such as diagnostic errors or errors in therapeutic judgment:

> The ongoing duty of a state medical board goes far beyond the licensing and ongoing registration of physicians. Boards also have the responsibility of determining when a physician's professional conduct or ability to practice medicine warrants modification, suspension, or revocation of a license to practice medicine. Boards safeguard the public by disciplining physicians who engage in unprofessional, improper, or incompetent medical practice.
>
> Boards review and investigate complaints and/or reports received from patients, other state medical boards, health professionals, government agencies and health care organizations about physicians who may be incompetent or acting unprofessionally, and take appropriate action against a physician's license if the person is found to have violated the law. State laws require that boards ensure fairness and due process to any physician under investigation.

[30] Understanding Medical Regulation in the United States, FSMB (last accessed Jan. 25, 2023), at https://www.fsmb.org/siteassets/education/pdf/best-module-text-intro-to-medical-regulation.pdf.

> Board members devote much time and attention to overseeing the practice of physicians. When a board receives a complaint about a physician, the board has the power to investigate, hold hearings and impose discipline, including suspension, probation or revocation of a physician's license, public reprimands, and fines.[31]

Thus, if a physician fails to adequately think through a diagnostic or treatment decision (i.e., by taking any recommendation at face value or other similar behavior, which FDA obviously fears will be the case), and if the physician can't blame the mistake on the performance of the software because the software was transparent regarding the basis for the recommendation and the fact that the software has limited accuracy, it is a matter for the state board of medicine to address, not FDA, under the Constitution. Even if the software recommendation is incorrect, if the software fully reveals the basis upon which it made the recommendation, the physician is responsible for thinking through and making the final decision. The fact that the software didn't get it right is not a defense that relieves the doctor of his or her professional responsibility.[32] But, again, this is under the state board of medicine's purview, not FDA's.

***b. Medical Malpractice***

States provide legal redress for medical errors through more than just the oversight by medical boards. States have elaborate medical malpractice laws that are designed to hold physicians and other health care professionals accountable for their decision-making.

Here, of course, the analysis needs to be fact specific. But if the developer of CDS software informs the user of the limitations of the software that impact accuracy and states that it should not be relied upon, and if the software makes available all of the information such that the physician can review it herself, the physician is the one that the state medical malpractice laws will hold responsible for any diagnostic or therapeutic decision-making errors.[33]

The point quite simply is that Congress knew what it was doing when it deferred to states to regulate medical decision-making, including such that is based on CDS software that is transparent enough that the user does not need to rely upon it in making decisions.

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[31] About Physician Discipline, FSMB (last accessed Jan. 25, 2023), at https://www.fsmb.org/u.s.-medical-regulatory-trends-and-actions/guide-to-medical-regulation-in-the-united-states/about-physician-discipline/.

[32] For Australia which has remarkably similar laws, here's a legal analysis: https://academic.pup.com/medlaw/advance-article/doi/10.1093/medlaw/fwac022/6646802.

[33] Smith, H. & Fotheringham, K., Artificial intelligence in clinical decision-making: Rethinking liability Medical Law International, Medical Law International (2020), at https://journals.sagepub.com/doi/full/10.1177/0968533220945766 (while written by British attorneys about the laws around the world generally, this article points out many of the factors that a court would consider in deciding how to allocate responsibility between the CDS software developer and the physician); *see also* Ridgely, M. Susan & Greenberg. Michael D., Too Many Alerts, Too Much Liability: Sorting Through The Malpractice Implications Of Drug-Drug Interaction Clinical Decision Support, Saint Louis University Journal Of Health Law & Policy (2012), at https://www.slu.edu/law/academics/journals/health-law-policy/pdfs/issues/v5-i2/ridgely_greenberg_article.pdf (offering a more U.S.-centric analysis).

## 7. FDA IS BREAKING THE LAW PROCEDURALLY

### *a. The Act and Good Guidance Practice Regulations Require FDA Guidance to Be Developed with Notice*

In 1997, Congress enacted the Food and Drug Administration Modernization Act ("FDAMA").[34] Section 405 of FDAMA, which added section 701(h) to the Act (21 U.S.C. 371(h)), provides in part:

> (C)(i) For guidance documents that set forth initial interpretations of a statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues, the Secretary shall ensure public participation prior to implementation of guidance documents . . . .

FDA's regulations at 21 CFR 10.115(g) then specifically require that the agency follow a notice and comment process to get input on a proposed guidance. The statute and the regulations were both the direct result of the undersigned filing a citizens petition on behalf of the Indiana Medical Device Manufacturers Council in 1995.

At issue here is whether the 2019 notice of the draft guidance is sufficient notice to support the CDS Guidance. To our knowledge, there is no case law specifically interpreting this provision of the good guidance practices, but, by analogy, the policy considerations are the same as for administrative notice and comment rulemaking. The purpose of the notice is the same in both regulatory procedures.

It is well established in the context of the federal rulemaking notice and comment process that the final rule needs to be a logical outgrowth of the proposal contained in the notice in order for the notice to have been adequate. Here is how one court recently described this basic concept:

> The requirement of notice and a fair opportunity to be heard is basic to administrative law." Chocolate Mfrs. Ass'n of U.S. v. Block, 755 F.2d 1098, 1102 (4th Cir. 1985). Notice must be "sufficiently descriptive to provide interested parties with a fair opportunity to comment and to participate in the rulemaking," but an agency "is not required to specify every precise proposal that it may eventually adopt as a rule." Kennecott v. EPA, 780 F.2d 445, 452 (4th Cir. 1985) (internal quotation marks omitted). The purpose of this procedure "is both to allow the agency to benefit from the experience and input of the parties who file comments … and to see to it that the agency maintains a flexible and open-minded attitude towards its own rules." Chocolate Mfrs. Ass'n, 755 F.2d at 1103 (internal quotation marks omitted). Under the APA, an agency is permitted to revise a final rule after initial notice of the proposed rule "if the changes in the original plan 'are in character with the

[34] P.L. 105-115 (1997).

> original scheme,' and the final rule is a 'logical outgrowth' of the notice and comments already given." Id. at 1105 (quoting BASF Wyandotte Corp. v. Costle, 598 F.2d 637, 642 (1st Cir. 1979)) (emphasis added). The proposed rule must enable the public "to discern what [is] at stake." Manufactured Hous. Inst. v. EPA, 467 F.3d 391, 400 (4th Cir. 2006). But "if the final rule 'substantially departs from the terms or substance of the proposed rule,' the notice is inadequate." Chocolate Mfrs. Ass'n, 755 F.2d at 1105 (quoting Rowell v. Andrus, 631 F.2d 699, 702 n.2 (10th Cir. 1980)).[35]

***b. The Final Guidance was Not a "Logical Outgrowth" of the 2019 Proposed Guidance***

With regard to this final CDS Guidance, the 2019 notice is plainly inadequate. Before getting into a substantive comparison of the topics raised in the proposal versus the topics raised in the final, frankly a simple visual comparison of the two highlights the enormity of the differences. Here we've used Microsoft Word to do the comparison, and that product has its own conventions for how it identifies changes. We did not include formatting changes. But the visualization is quite stark and is included as Appendix A.

We note also that FDA does not have the excuse of needing to move quickly to a final draft. We say this because the final draft came six years after the Cures Act became effective, and three years from the most recent draft. FDA apparently wasn't in a hurry, which leaves us additionally perplexed as to why the agency would not have reproposed its new intentions.

The traditional analysis a court would engage in would be to compare substantive concepts between the proposed and final documents. We provide here a high-level summary of the differences conceptually between the two documents, in no particular order:

1. The proposed guidance includes several pages of discussion of the International Medical Device Regulators Forum ("IMDRF") risk stratification framework and then employs that risk framework as the fundamental paradigm for deciding what software gets regulated and what does not. That framework was completely dropped in the final CDS Guidance.

2. The final CDS Guidance removed all discussion of enforcement discretion applied to software used by patients and caregivers. There were a couple of tables in the proposed guidance that have been removed in the CDS Guidance, as well as a discussion that was on page 16 of the draft, under the heading "Policy for Device CDS Function", which applied a risk-based approach to allow enforcement discretion to be applied to software intended for use by patients and caregivers. All of that is gone in the CDS Guidance.

[35] Ctr. for Sci. in the Pub. Int. v. Perdue, 438 F. Supp. 3d 546 (D. Md. 2020).

3. In the final CDS Guidance, FDA has now inserted a definition—completely new—of the term "health care professional" in footnote 1. The definition is significant in that it lists a variety of professions that FDA now deems to be part of that term.

4. Regarding the first criterion of the Cures Act, FDA added completely new discussion of:

   a) A definition of "medical image."

   b) A definition of "pattern", a definition that turns out to be very important throughout the rest of the document because FDA repeatedly asserts that software it wants to regulate makes use of patterns.

   c) Language that would preclude software that includes functions that "assess or interpret the clinical implications" of a signal, pattern, or medical image. That is a pivotal requirement of CDS software.

5. Continuing FDA's theme of adding definitions that are anything but intuitive or well accepted, and indeed in many cases violate the Cures Act as explained more below, FDA added the following under criterion number two:

   a) A definition of "medical information about a patient" that includes very limiting language to those types of information that are already well accepted and often communicated among professionals when discussing the topic, in violation of the Cures Act.

   b) A definition of "medical information" that includes very limiting language that would require all such information to meet certain quality standards associated with peer review, in violation of the Cures Act.

   c) Many new examples of what FDA would consider acceptable and unacceptable information.

6. Under criterion three, FDA took two short paragraphs that were less than half of a page and blew them up to three full pages that include many new concepts and a new list of examples worthy of soliciting comment, including:

   a) The level of software automation;

   b) The concept of automation bias (The proposed guidance included no discussion of automation bias, where the CDS Guidance incorporated a substantial and pivotal discussion of automation bias as the factual foundation for the changes FDA wanted to make. In footnote 10, FDA referenced experience at the Federal Aviation Administration with automation bias. This is a highly technical matter that would have benefited greatly from public comment before it became the basis for an FDA policy. The public, including medical experts, could have weighed in on whether there are important differences between the practice of medicine and the activity of aviation.);

c) The time critical nature of the decision-making, in violation of the Cures Act as explained more below;

d) A three-part conceptual description of what qualifies under the criterion;

e) A four-part description of what does not qualify under the criterion; and

f) Broad language to exclude software that provides information "that a specific patient 'may exhibit signs' of a disease or condition or identifies a risk probability or risk score for specific disease or condition is providing a specific preventive, diagnostic or therapeutic output." Absolutely none of that was in the proposed guidance.

7. With regard to criterion four, FDA took four sub-criteria that required a total of four lines in the text, and dramatically expanded them to occupy 27 lines of the text. The new text is substantively quite different, and includes concepts like imposing the time critical limit, requiring that the developers explain how the inputs are obtained and the quality requirements for those inputs, a description of the algorithm, significant details about the validation performed and a much more in-depth discussion of the software output specifications.

8. At the end of the document, FDA completely revamped the examples which, frankly, are where the real clarity comes from guidance documents for industry. In its changes, the FDA added many new examples, dropped many former examples, and where it carried over the examples, substantially rewrote them. There is almost no similarity between the final set of examples and the ones previously proposed.

In many ways it would have been easier to explain where the two documents retained similarity. The only real similarities were in some of the introductory material that is consistent across all FDA guidance documents, not unique to the CDS guidance documents at issue.

It may be hard to fathom exactly just how significant the qualitative differences described above are. Making use of modern data science techniques, we calculated the Jaccard similarity between the 2019 draft and the 2022 final. If you are not familiar with the concept of Jaccard similarity, it is a mathematical way of comparing differences in text. If you would like to read more about it, the undersigned published a blog post in his February 2023 monthly column on Unpacking Averages. The Jaccard similarity of the two documents is 0.346.[36]

As points of reference, the blog post includes the Jaccard similarity of the proposed versus final draft of three other similar guidance documents. To interpret a Jaccard similarity number, you need to understand that a Jaccard similarity of 1.0 reflects absolutely identical documents, where

[36] Bradley Merrill Thompson,, Unpacking Averages: Using NLP to Assess FDA's Compliance with Notice and Comment in Guidance Development Health Law Advisor (Feb.1, 2023), at https://www.healthlawadvisor.com/2023/02/01/unpacking-averages-using-nlp-to-assess-fdas-compliance-with-notice-and-comment-in-guidance-development/.

a Jaccard similarity of 0.0 reflects completely different documents with not a single word in common.

As explained more in the referenced blog post, the difference is surprising. We would have guessed that the three other guidance documents would have been a greater distance between draft and final because the CDS Guidance went through the extra step of a re-proposal, which should have, in theory, brought it closer to the final draft. Further, the three other guidance documents were written in an area where FDA had wide discretion to choose its preferred policy, where the CDS Guidance is supposed to be simply a faithful interpretation of a statute.

The new content without a doubt would have benefited from public input. The new content raises almost entirely different questions from the proposed. Therefore, FDA did not provide sufficient notice for the CDS Guidance.

## 8. FDA IS BREAKING THE LAW SUBSTANTIVELY

### *a. Basic Principles of Statutory Construction and Agency Deference*

Agencies must read and apply statutes as written. When they do, courts will accord them a certain amount of deference. However, that deference is only granted when the agency follows certain procedures to promulgate rules. According to Statutory Interpretation: General Principles and Recent Trends:

> Under current precedent, when a court reviews an agency's formal interpretation of a statute that the agency administers, and when the statute has not removed agency discretion by compelling a particular disposition of the matter at issue, courts defer to any reasonable agency interpretation. This is the Chevron rule announced in 1984. In two decisions, one in 2000 and one in 2001, the Court clarified and narrowed Chevron's application, ruling that Chevron deference applies only if an agency's interpretation is the product of a formal agency process, such as adjudication or notice and comment rulemaking, through which Congress has authorized the agency "to speak with the force of law." Other agency interpretations that are made without a formal and public process often are reviewed under pre-Chevron principles set forth in Skidmore v. Swift & Co . . . .
>
> As in other matters of interpretation, it is congressional intent that counts. Under Chevron, the first question is "whether Congress has directly spoken to the precise question at issue." If the court, "employing the traditional tools of statutory construction," determines that Congress has addressed the precise issue, then that is the end of the matter, because the "law must be given effect." However, if the statute does not directly address the issue, "the court does not simply impose its own construction of the statute," but

> rather determines "whether the agency's answer is based on a permissible construction of the statute."[37]

FDA's interpretation of the statute at issue, the Cures Act, is not permissible and ignores congressional intent as evidenced in the statute itself.

Above we argue that, procedurally, the notice required for administrative rulemaking is similar in purpose to the notice required for guidance development. While that is true, it is also true that a court would not give guidance the same respect as rulemaking. According to Statutory Interpretation: General Principles and Recent Trends:

> Agency interpretations that take place in the many less formal contexts where Chevron deference is inapplicable (e.g., opinion letters, policy statements, agency manuals, and enforcement guidelines, "all of which lack the force of law") can still be "entitled to respect," "but only to the extent that [they] have the power to persuade." As the Court put it in Skidmore v. Swift & Co., agency interpretations "constitute a body of experience and informed judgment to which courts and litigants may properly resort.... The weight of such a judgment in a particular case will depend upon the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control." These factors may include whether an interpretation applied technical expertise on a complex matter within agency jurisdiction, whether an agency's decision was well-reasoned, and whether the agency's interpretation was longstanding or consistent.[38]

For evaluating FDA's interpretation of the Cures Act as expressed in the final CDS Guidance, FDA's interpretation will only carry the day if it is persuasive and consistent with the statute. We believe it is neither.

We are entitled to use all the normal rules of statutory construction to interpret what the existing statute says. For all the reasons explained below, a court would reject FDA's CDS Guidance as an improper interpretation of the Cures Act.

### *b. Examples of FDA Ignoring the Statute*

The following are just a few of the clearer examples of where FDA materially departs from the statute and, indeed, violates its terms.

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[37] Statutory Interpretation: General Principles and Recent Trends, EveryCRSReport (Sept. 24, 2014), at https://www.everycrsreport.com/reports/97-589.html#_Toc407006241.

[38] *Id*.

*i. FDA unlawfully interprets the simple phrase "medical information about a patient."*

Criterion 2 of the Cures Act requirements for CDS is that the software is not a device if it is "intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines)." The "plain meaning rule" holds that where the language of a statute is plain, the sole role of the courts is to enforce it according to its terms.[39] To depart from or to supplement a statutory interpretation, the words have to first be found to be ambiguous. The CDS Guidance makes no attempt in its discussion of Criterion 2 to articulate any ambiguity concern regarding the statutory language. Instead, the necessary conclusion is that FDA simply wants to graft on what it would prefer the policy to be over what Congress wrote.

As provided above, the Cures Act says that CDS developers can produce unregulated software that analyzes "medical information about a patient." In the CDS Guidance, FDA interprets those five words to mean "the type of information that normally is, and generally can be, communicated between HCPs in a clinical conversation or between HCPs and patients in the context of a clinical decision, meaning that the relevance of the information to the clinical decision being made is well understood and accepted." Congress did not so limit this exemption as to include only information that is commonly discussed. If Congress had meant to include that restriction, Congress could have easily said so.[40] In other places in the FD&C Act where Congress intended to impose a restriction, Congress plainly included the restriction in the statute. Consider, for example, the statutory definition of a "food additive" that excludes foods generally recognized as safe. In that instance, in section 201(s) of the FD&C Act, the statute explains that an article will be a regulated food additive "if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures … to be safe under the conditions of its intended use." Congress has no problem writing restrictive definitions that invoke general recognition when it wants to.

The Cures Act language for Criterion 2 simply says, "medical information about a patient." What could be clearer? We think it is particularly revealing that FDA went through two different draft

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[39] Harbison v. Bell, 556 U.S. 180, 198 (2009) (Thomas, J., concurring).

[40] Central Bank of Denver v. First Interstate Bank, 511 U.S. 164, 176–77 (1994). *See also* Franklin Nat'l Bank v. New York, 347 U.S. 373, 378 (1954) (finding "no indication that Congress intended to make this phase of national banking subject to local restrictions, as it has done by express language in several other instances"); Meghrig v. KFC Western, Inc., 516 U.S. 479, 485 (1996) ("Congress . . . demonstrated in CERCLA that it knew how to provide for the recovery of cleanup costs, and . . . the language used to define the remedies under RCRA does not provide that remedy."); FCC v. NextWave Personal Communications, Inc., 537 U.S. 293, 302 (2003) (when Congress has intended to create exceptions to bankruptcy law requirements, "it has done so clearly and expressly"); Dole Food Co. v. Patrickson, 538 U.S. 468, 476 (2003) (Congress knows how to refer to an indirect owner of a corporation, as distinct from a direct owner of shares in the "formal sense," and did not do so in the Foreign Sovereign Immunities Act's definition of foreign state "instrumentality"); Whitfield v. United States, 543 U.S. 209, 216 (2005) ("Congress has included an express overt-act requirement in at least 22 other current conspiracy statutes, clearly demonstrating that it knows how to impose such a requirement when it wishes to do so."); Mississippi ex rel. Hood v. AU Optronics Corp., 571 U.S. ___, No. 12-1036, slip op. (Jan. 14, 2014) (when Class Action Fairness Act authorizes removal of a state case to federal court as a "mass action" if the case was brought by 100 or more persons, only named plaintiffs may be counted; in the same statute, Congress explicitly had included counting "unnamed parties in interest" toward meeting class action thresholds and could have done so under the mass action provision if it so chose.).

guidance documents, in 2017 and 2019, without any problem reading that phrase and without the need to provide clarification. The flawed interpretation was only raised in the third iteration of the guidance document, the CDS Guidance.

To interpret the phrase "medical information about a patient" the way FDA does in the CDS Guidance is to severely tie the hands of algorithm developers in a way that Congress did not intend. Machine learning developers routinely include other information adjacent to classical diagnostic information to improve accuracy. The Cures Act CDS language for Criterion 2 in no way says that the information must be limited to that which we already know is relevant.

*ii. FDA interprets the phrase "or other medical information" as a restriction, when it is plainly meant to enlarge the information that falls within the criterion.*

Following the phrase "medical information about a patient", the Cures Act says that CDS developers can develop software that analyzes "other medical information." In normal English language, that is open-ended and *expands* the idea of what kind of information can be used as the basis for algorithm development. Yet FDA takes it in the complete opposite direction, declaring that those are words somehow of limitation, words that mean the information must be from peer-reviewed clinical studies, clinical practice guidelines or "similarly independent and verified and validated as accurate, reliable, not omitting material information and supported by evidence." The phrase "such as" does not impose a restriction.

Again, agencies are supposed to take the words Congress gives them and read them plainly. The Cures Act provides no such support for FDA's interpretation, merely offering a couple of items as examples, not as limitations.

Note that the parenthetical phrase following the phrase "or other medical information" should not be confused with the case of where general words follow an enumeration of specific items. In the case at hand, a general phrase is followed by a parenthetical that simply provides a few examples not meant as a limitation.

The *ejusdem generis* rule states that where "general words follow enumerations of particular classes or persons or things, the general words shall be construed as applicable only to persons or things of the same general nature or kind as those enumerated".[41] Thus in this case, the "or other medical information" needs to be read in light of the item that preceded it: namely "medical information about a patient." It is meant to amplify on that term and be guided by the meaning of that term. Thus, all medical information should be about patients. But the parenthetical that comes after does not restrict, but merely provide examples for context.

*iii. Saying that a "Recommendation" cannot be specific is flawed.*

Criterion 3 of the Cures Act requirements for CDS is that the software is not a device if it is "intended for the purpose of supporting or providing recommendations to a health care

[41] Walling v. Peavy-Wilson Lumber Co., 49 F. Supp. 846, 859 (W.D. La. 1943) (involving interpretation of the words "board, lodging, or other facilities").

professional about prevention, diagnosis, or treatment of a disease or condition." Words that are not terms of art and that are not statutorily defined are customarily given their ordinary meanings, frequently derived from the dictionary.[42] According to Oxford Languages and Google,[43] the word "recommendation" means "a suggestion or proposal as to the best course of action, especially one put forward by an authoritative body." A couple of things are noteworthy about the definition. First, it does not require multiple options be presented. It simply says, "a suggestion or proposal." And second, the definition suggests that the recommendation can have weight behind it, the kind of weight that comes from an authoritative body. It does not have to be mealymouthed, vague, or otherwise nonspecific.

FDA, in contrast, interprets those words in Criterion 3 as meaning that the software output cannot be intended to "direct" health care professionals what to do. FDA does not provide any statutory argument to support its reading that, somehow, the word recommendation means that the language cannot make a specific proposal for the health care professional to consider. Instead, for the first time out of all of the iterations of the guidance documents, FDA merely introduces the new concept of automation bias that it borrowed from aviation, as discussed above. That concept, whatever its merit, cannot justify departing from what Congress specifically said in the statute.

As already observed, the word recommendation specifically means providing a singular proposal from an authoritative source. That is what makes a communication into a recommendation, as opposed to providing a brainstorming laundry list of possibilities. FDA's reading is actually the opposite of what Congress said in the statute.

It is telling that FDA took this approach in connection with Criterion 3, which involves simply any recommendation provided by software, as opposed to Criterion 4 which speaks specifically about the need for reliance. FDA wanted to substitute its absolute bar for certain types of software in lieu of the congressional test of making the basis available to the health care professional user so that there is no need for reliance. In our opinion, FDA can argue that the time critical element of the decision-making can be factored into the analysis under Criterion 4; but FDA apparently disfavors that because it would allow for judgment to be exercised, as opposed to an absolute bar.

*iv. FDA's efforts to enlarge its jurisdiction at the expense of states would have to be expressly authorized by Congress.*

The collective effect of FDA's reading of the Cures Act is to expand its jurisdiction into territory that Congress plainly left for the states to regulate. As already noted, Congress defers the practice of medicine to state boards of medicine out of respect for the states and the Constitution. As a result, FDA's expansive reading of the Cures Act as documented in the CDS Guidance would be disfavored by any reviewing court. A basic canon of statutory interpretation holds that "the assumption that the historic police powers of the States were not to be superseded by [a federal

[42] In the absence of a statutory definition, "we construe a statutory term in accordance with its ordinary or natural meaning." FDIC v. Meyer, 510 U.S. 471, 476 (1994). *See also*, *e.g.*, Mohamad v. Palestinian Authority, 566 ___, No. 11-88, slip op. (April 18, 2012) ("individual," as used in the Torture Victim Protection Act, does not include an organization).

[43] Google's English dictionary is provided by Oxford Languages.

law] unless that was the clear and manifest purpose of Congress."[44] A court would not allow FDA to intrude by regulating the practice of medicine unless the statute was very clear that Congress intended that outcome. There is no such evidence here. Quite the contrary.

## 9. PRACTICAL PROBLEMS FOR INDUSTRY

FDA's final CDS Guidance will choke off much of the supply of innovative CDS software to the ultimate detriment of the patients who need care. In Section 2 above, we went through many of the benefits that CDS offers the health care industry. The problem is the final CDS Guidance puts many obstacles in the way of developing that helpful CDS software. Here are just a few of the obstacles that the CDS Guidance erects for software developers who lack the considerable resources necessary to go through the FDA approval process:

- It is very common, particularly when machine learning is being used, for developers to use data not traditionally considered in a diagnostic or therapeutic decision. In practice, this is how developers achieve successful accuracy. Thus, under the CDS Guidance, developers will either have to leave out that additional data, thereby reducing the accuracy of the machine learning model, or give up on developing the CDS software altogether.
- Requiring multiple possible diagnostic or therapeutic interventions is not always possible, because sometimes the right approach becomes quite clear early on in the process. Gratuitously adding other possibilities only becomes a source of confusion, not clarity or assistance. It hurts patients rather than helps them.
- The final CDS Guidance would seem to prohibit providing even multiple options that are each associated with a given likelihood of success, due to the language at the bottom of page 12 that would cause the following to be FDA regulated: "software that . . . identifies a risk probability or risk score for a specific disease or condition." Physicians need that statistical information and withholding it compromises the quality of their decisions, instead of enhancing it.
- FDA seems to want to discourage automation in CDS software, which is tantamount to preferring to row the steamship. The agency's premise is a very paternalistic and cynical view regarding the decision-making capabilities of health care professionals.
- Further, FDA completely ignores the problem of human error, as if automation error is the only risk here. Automating certain mechanical tasks is a way to improve quality, and FDA is actively discouraging it, encouraging developers instead to produce pedestrian software that accomplishes very little.
- Under the CDS Guidance, time critical decision making is a bar to bringing CDS software products to market under the exemption, rather than as a factor to consider during development. A huge amount of medicine is time critical—for example, many of the decisions made in an emergency department or even urgent care, which have historically been sites of care that require more use of CDS software because of the diversity of symptoms presented. Denying those sites of service access to exempt CDS software will dramatically lessen the current quality of care being delivered in those sites.

[44] Rice v. Santa Fe Elevator Corp., 331 U.S. 218, 230 (1947); Wisconsin Public Intervenor v. Mortier, 501 U.S. 597, 605 (1991). *See also* Medtronic Inc. v. Lohr, 518 U.S. 470, 485 (1996) ("[B]ecause the States are independent sovereigns in our federal system, we have long presumed that Congress does not cavalierly pre-empt state-law causes of action.").

- The CDS Guidance hurts the U.S.-based CDS software developers who are naturally focused on the U.S. market. The European Commission's AI Act, for example, takes a risk-based approach to regulating CDS which will allow CDS developers in the European Union to thrive. Once the U.S. market finally opens, those foreign manufacturers will be able to flood the U.S. market with their products to the detriment of U.S.-based innovation.

We recognize that some at FDA might argue that guidance is merely guidance, not a rule, and that if anyone disagrees with the CDS Guidance they are free to do as they see fit under the law. We certainly hope that people at FDA do not think that way. If that were true, it would mean that guidance provides no value because it does not need to be accurate and no one, including FDA, should put much effort into it. But, more than that, FDA surely realizes that most companies do not have the financial resources to individually contest FDA. These businesses must go along with what FDA says. So, if FDA takes a position that is contrary to the law, the vast majority of medical device companies will have no choice but to abide by it.

The bottom line is that because of the CDS Guidance, many CDS projects will just get shelved to the ultimate detriment of the patient, or at best they will get watered down into general wellness products that do not have the features or labeling necessary to truly make a difference on health care.[45]

## 10. IMPACT ON FDA'S LAW ENFORCEMENT MISSION

Beyond the impact on industry described above, the FDA's CDS Guidance will have a severe impact on its own ability to enforce the FD&C Act. We will offer three negative consequences for the agency itself.

### *a. FDA's Ability to Enforce the Act Will Be Diminished*

FDA does not have the resources to comprehensively enforce all of the requirements of the FD&C Act. Just as the Internal Revenue Service relies on the millions and millions of taxpayers to honorably calculate their taxes each year, and only has the resources to audit a small fraction of those, FDA needs to rely upon the honorable compliance of medical device developers.

As much as we would like to believe that everyone just wants to do the honorable thing, we suspect FDA knows there are companies out there that on a daily basis face the temptation to skirt the rules. They face that temptation because they see competitors violating the rules, and because the free market punishes those with higher costs, often companies will be tempted to ignore rules.

Here is what FDA may not fully appreciate: Fortunately, regulatory affairs professionals and attorneys are engaged by medical device companies to act as the conscience of the company, and to urge the company to comply with the law. When asked why they should comply when their competitors do not, the attorney or regulatory affairs professional will respond that following the

[45] *See, e.g.*, Cohen, I. Glenn, Shachar , Carmel, & Simon, David, Skating the line between general wellness products and regulated devices: strategies and implications, Journal of Law and the Biosciences (July 14, 2022).

law is simply the right thing to do. It is the moral thing, even though it is not the expedient or low cost option. These professionals appeal to the belief in the rule of law.

Then FDA goes and does something like this. FDA, the very organization tasked with enforcing the law, flagrantly violates the law. FDA may have its own self-serving reasons for wanting to do it, and the agency may feel morally justified somehow, but the fact of the matter is FDA is ignoring the rule of law.

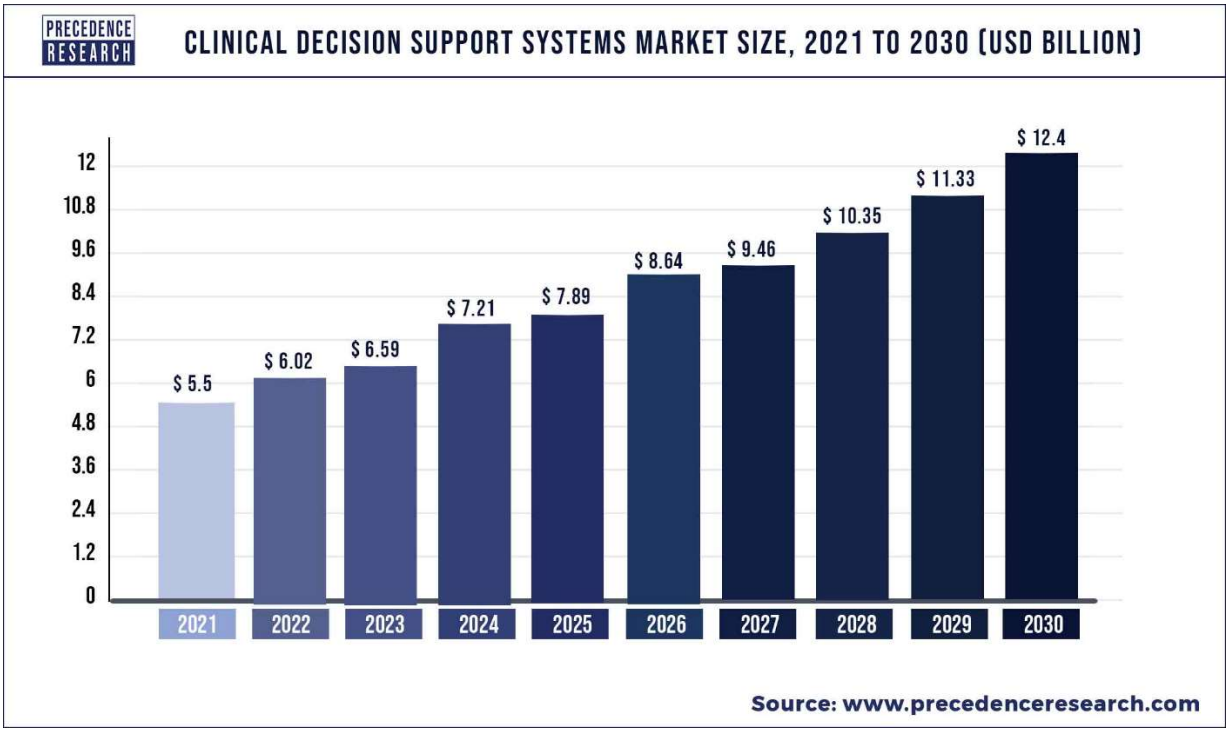
The effect is highly corrosive on voluntary compliance by companies. How can regulatory affairs professionals and attorneys, with a straight face, look company management in the eye and tell them that they ought to follow the law even though the competitors are not, *and even though the very federal agency tasked with enforcing the law is itself obviously violating the law*. It simply shakes everyone's confidence in the rule of law itself and makes company representatives question the point of compliance.

The federal government has to stop violating the law if it wants American society to abide by the rule of law. It is really just that simple.

***b. FDA Will Be Overwhelmed with Regulatory Submissions, Probably De Novos***

The FDA cannot effectively predict the number of products on the market currently combined with those planned for the future that would be captured by unnecessary regulation by the final CDS Guidance. In the absence of complete data, we will need to make some assumptions.

First, we start with the recognition that the CDS industry is large and growing at a quick rate. There are literally dozens of estimates out there, and here is one projection of the global market:



You can read a summary of the report by Precedence Research, which is publicly available.[46] North America is estimated to be 46% of the estimated projections.

The data presented, though, actually understates the size of the industry because it does not include hospital-developed CDS software. The CDS figures given above for the growth of the industry only account for CDS software products sold by vendors to customers—they do not include internally developed CDS software at hospitals and other large health care providers that is then made generally available. The problem for policymakers is that such software is not tracked by market research firms, so we have no data on exactly how many such products are out there.

As FDA knows, even though hospital developed CDS software is not included in the market research we recited above, there is a good chance that FDA will regulate at least a portion of that market. FDA's guidance on Policy for Device Software Functions and Mobile Medical Applications[47] explains that FDA regulates software that is developed by large health care providers and then made available. That guidance states that the following are unregulated, but with the specified exemption:

> [I]f Dr. XYZ, a licensed practitioner, creates a mobile medical app called the "XYZ-recorder" that enables attaching an ECG electrode to a smartphone, and provides the "XYZ-recorder" to his/her patient to use it to record the patient's electrocardiographic readings for 24 hours, Dr. XYZ is not considered a mobile medical app manufacturer. If Dr. XYZ is in a group practice (including a telehealth network) and permits other physicians in the practice to provide the XYZ-recorder to their patients, Dr. XYZ is not considered a mobile medical apps manufacturer. <u>However, if Dr. XYZ, the licensed practitioner, distributes the "XYZ-recorder" and, through labeling or promotion intends to make it generally available to or to be generally used by other physicians (or other specially qualified persons), Dr. XYZ would be considered a mobile medical app manufacturer.</u>[48]

Group practice does not typically include hospitals or HMOs, to name a few.[49] If FDA follows that CDS Guidance, the burden on FDA resources becomes even worse because many hospitals and health systems are developing such CDS software for general use even though it is not captured

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[46] Clinical Decision Support Systems Market, Precedence Research (Oct. 2022), at https://www.precedenceresearch.com/clinical-decision-support-systems-market#:~:text=The%20global%20clinical%20decision%20support,and%20integrated%20reliable%20technical%20solutions; *see also* Clinical Decision Support Systems Market Size, Share & Trends Analysis Report By Product, Market Analysis Report, Grand View Research (2020), at https://www.grandviewresearch.com/industry-analysis/clinical-decision-support-system-market.

[47] Policy for Device Software Functions and Mobile Medical Applications, FDA Guidance for Industry and Food and Drug Administration Staff (Sept. 2022), at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-device-software-functions-and-mobile-medical-applications.

[48] *Id*. (*emphasis added*).

[49] Medicare defines "group practice" at 42 CFR 411.352.

in the market research we shared above. Again, to be clear, the market research shared in this Petition *understates* the scope of what FDA will end up regulating.

The tougher question is how many of the current and future CDS software products will be negatively impacted by FDA's CDS Guidance. Admittedly, we lack good data on this point, but FDA lacks data as well. We recognize that it would be useful to have data that would identify, even roughly, the percentage of the U.S. CDS market that would be negatively affected by this guidance. In the coming months we will try to devise an appropriate methodology to collect at least a representative sample of the universe of CDS software, and then evaluate that sample through the lens of the final CDS Guidance to assess its impact. If we are able to do that it will take time, so we are submitting this Petition now and will supplement it if and when we can collect that data.

As a result, although we cannot put a precise number to it, we anticipate that there would be a significant bolus of companies that need to get FDA clearance for existing products, and a rather large uptick in the number of companies in the future that would have to get FDA approval of some sort.

Based on our knowledge of the existing product classifications that potentially apply to CDS software, we anticipate that a large share of these future submissions will be through the de novos pathway. Many companies are planning more novel and innovative CDS solutions, and that novelty would typically put them in a de novo category. As FDA knows well, the significance is that such submissions require far more FDA resources than 510(k) submissions, even with user fees.

We do not think FDA will be able to handle the bolus and, as a result, submissions of all sorts, not just CDS, will languish.

### *c. FDA will waste precious resources and duplicate the efforts of the states*

Following the CDS Guidance will require more than just agency review resources, it will require enforcement resources, as well as other agency resources, to extend a variety of other FDA regulatory requirements that apply to medical devices. Based on all the information provided above that demonstrates that there is no public health risk associated with these CDS products, FDA expenditure of these resources will be a waste.

Further, as explained above, the states are already regulating the practice of medicine which includes medical decision-making. FDA's efforts here will amount to duplication of those state level efforts, which not only frustrates the Constitutional division of responsibility, but wastes federal resources.

As we understand from FDA's requests for resources from Congress, FDA does not have extra resources to waste in this regard.

## 11. IMPACT ON THE PUBLIC HEALTH

We saved the most important concern for last. FDA's action will harm the public health.

In writing section 3060 of the Cures Act, as in writing any section of the FD&C Act, Congress balanced the benefits of regulation with the cost of regulation. As virtually everyone is aware, regulation costs in many different ways. Overregulating carries with it a negative impact on the public health which FDA is supposed to be advancing. We will summarize the three ways those negative effects are felt.

### *a. Slowing The Speed to Market for Innovative CDS*

As we have already outlined above, many CDS developers will simply abandon their efforts to bring CDS software products to market. But, in addition to that, for those who decide to persist nonetheless and obtain the necessary FDA clearance or approval, imposing the regulation described in the CDS Guidance on them will slow the speed to market. We are not plowing any new ground here. This is a well-recognized impact of extending FDA's jurisdiction over previously unregulated products.

What makes this delay even worse, though, for CDS software as compared to other medical devices is the fact that FDA does not have a practical regulatory paradigm for software generally that requires modifications persistently over time. Also, the current FDA regulatory system does a poor job of bringing to market software that employs machine learning where the algorithm is constantly improving over time. FDA abandoned its pilot project for precertification and has not yet come out with its guidance for predetermined change control plans. FDA is simply not in a position to efficiently and swiftly regulate software, in particular software that employs machine learning.

As already noted, what makes this worse yet is the fact that FDA does not have appropriate product codes for much of the innovative CDS software products currently being developed or envisioned for the future. This means that developers will have to follow the de novo route, which again is particularly fraught with delays and costs. The average review time for the de novo pathway is well over twice that of the 510(k) pathway.[50]

There is no doubt that FDA regulation, including especially premarket review, slows down a product's path to market: in fact, it is designed to do just that. The question is whether any of the benefits of FDA regulation outweigh that cost. Congress weighed these issues and rendered its decision. It is not for FDA to override that balancing, to the detriment of patients.

### *b. Discouraging Innovation in CDS That Potentially Improves the Quality of Care*

This topic was discussed above in the context of injury to industry, but that impact is only an intermediate step toward the ultimate negative impact to patients. Above we outline the considerable benefits of CDS software, and we outline the evidence suggesting very little risk as

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[50] FDA's Agenda for Quarterly Meeting on MDUFA IV (FY 2018-2022) Performance at https://www.fda.gov/media/163306/download.

officially assessed by FDA. Chilling innovation in the CDS space by imposing government regulation cannot be justified on the evidence.

***c. Imposing Costs on Those Developing CDS, That Must Be Passed Along Ultimately to The Patient, Which Also Limits Access***

Out of technology generally, software-only products have fewer barriers to entry because they do not require the same upfront capital investment to build, for example, a manufacturing plant. As a result, much software, especially CDS, comes out of university research that is spun out into startups. A conference on FDA regulation of artificial intelligence and CDS organized by the undersigned at six major engineering schools across the country attracted over a thousand attendees. The universities are engines of innovation in this space.

However, much university-invented CDS software will never see the light of day if the developers must undergo the FDA marketing requirements. Thinly capitalized or venture backed startups will often not have the financial staying power to weather the process of securing FDA approval for their technologies. For those who do succeed, it will be because they have to spend quite a bit more time and money on their software to satisfy the FDA requirements, and they will have to pass those costs along ultimately to the users, whether directly through pricing or indirectly through insurance purchased by employers. Those costs will reduce access to the information they provide.

## C. Environmental Impact

Petitioner claims a categorical exclusion from the requirements for an Environmental Assessment under 21 C.F.R. § 25.30(h).

## D. Economic Impact

Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

## E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioner that are unfavorable to the Petition.

Submitted by,

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