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Deeva V. Shah

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NOTE

THE OVERSIMPLIFICATION OF DEREGULATION: A CASE STUDY ON CLINICAL DECISION SUPPORT SOFTWARE

Deeva V. Shah

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ABSTRACT

Until the December 2016 passage of the Cures Act, the FDA had regulatory power over clinical decision support (CDS) software; however, the Act removed a large group of CDS software from the FDA's statutory authority. Congressional intent was to increase innovation by removing regulatory blockades—such as device testing and certification—from the FDA's purview. This note argues that the enactment of this specific provision of the Act will instead stymie innovation and overlook the unfortunate safety consequences inherent in its deregulation. CDS software is a burgeoning field ripe for innovation; however, rapid innovation can often lead to a slew of mistakes—mistakes in software coding, mistakes in software implementation, and even mistakes in software design. This note considers the issues with deregulating CDS software, focusing on the health and safety concerns, as well as the lack of incentive for software creators to share algorithms. This note then proposes other, less-invasive regimes for CDS software regulation to address these problems.

INTRODUCTION

In December 2016, Congress passed, and the President signed into law, the 21st Century Cures Act (Cures Act).¹ While the Cures Act has a range of provisions targeting FDA review and approval of both drugs and medical devices, this Note focuses on Section 3060, titled 'Clarifying Medical Software Regulation.'² Until the passage of the Cures Act, the FDA had

1. Katie Reilly, *Watch Live: President Obama Signs the 21st Century Cures Act*, TIME MAGAZINE (Dec 13, 2016), <http://time.com/4599295/president-obama-cures-act-livestream-online/>.

2. 21st Century Cures Act, Pub. L. No.114-255, 130 Stat. 1034, 1130-33 (2016).

assumed regulatory power over clinical decision support (CDS) software under the FDA's jurisdiction over medical devices.³ CDS software includes software with big data algorithms used to direct physicians to tailored treatment options and verify drug-drug and patient-drug reactions. The Cures Act removes a large group of CDS software from the statutory definition of 'device,' thus removing CDS software from the FDA's jurisdiction.⁴ By removing such critical technology from FDA regulation, Congress intended to increase innovation by removing regulatory blockades; however, this Note argues that Congress' enactment of the Cures Act has instead both stymied innovation and overlooked the safety consequences inherent in its deregulation.

Part I of this Note explores the history of CDS software, explaining what CDS software is and how the FDA has regulated such software in the past. Part II looks at the changes to CDS software regulation under the 21st Century Cures Act. Part II also considers the rationales behind deregulating CDS software and why the Cures Act, specifically the CDS provision, was passed without much resistance. Part III considers two major issues with deregulating CDS software and removing it from the FDA's regulation. Part III initially analyzes the health and safety concerns surrounding the use of CDS software, especially concerns related to human error and alert fatigue. Then, Part III looks at the lack of incentive for software creators to share algorithms, especially without FDA regulation. Part IV argues that FDA regulation involving minimum safety standards for CDS and a pre-approval regime of regulatory exclusivity would be a better option to address public health concerns and to ensure ongoing innovation.

I. CLINICAL DECISION SUPPORT SOFTWARE: A DISCUSSION OF PAST REGULATION

Clinical decision support software (CDS) refers to electronic technology used to enhance clinical decision-making.⁵ CDS combines electronic health records, e-prescribing systems, computerized physician order entry, medication reconciliation systems, and symptom trackers to help clinicians in their work.⁶ CDS can help a clinician "reach proper diagnoses, ask the right questions, and perform appropriate tests on the front end of the decision-making process—preventing errors of omission—as well as stop errors of commis-

3. Greg Slabodkin, *21st Century Cures Act clarifies FDA regulation of software*, HEALTH DATA MANAGEMENT (Dec. 5, 2016, 6:57 AM), <https://www.healthdatamanagement.com/news/21st-century-cures-act-clarifies-fda-regulation-of-software>.

4. 21st Century Cures Act § 3060(a)(1).

5. *Clinical Decision Support (CDS)*, HEALTHIT.GOV, <https://www.healthit.gov/policy-researchers-implementers/clinical-decision-support-cds> (last visited Dec 13, 2016).

6. *See generally Id.*

sion on the back end, during treatment and procedures.⁷⁷ CDS proponents describe CDS as a process for enhancing a physician's health-related decisions with pertinent, organized clinical knowledge and patient information to improve health and healthcare delivery.⁸

CDS can take multiple forms. The most common is a computerized, physician-ordered entry system (a typical database entry system used by hospitals) with an integrated CDS as an electronic layer of review.⁹ This layer frequently supports physicians in the process of ordering prescriptions by alerting physicians to any critical drug-patient and drug-drug interactions.¹⁰ Ordered entry systems, like UpToDate, not only aggregate and report the latest research, but they also synthesize the evidence and provide point-of-care recommendations.¹¹ This basic form of CDS software provides alerts to clinicians as they refill prescriptions and can remind clinicians to alter or update drug dosages, change the timing for administering medicine, and provides alternative options if a certain drug is not working.

There are more advanced forms of CDS that go beyond the basic alerts found in UpToDate and other prescription-based CDS systems. For example, the Clinical Assistant by Grand Round Table combines electronic health records with big data analysis on a personalized, individual basis.¹² The Clinical Assistant "uses the information the clinicians have already entered about their patients . . . and [the patients'] test results to generate a deidentified clinical profile. The Clinical Assistant then delivers distilled insights. . . by pattern matching that profile against a database of millions of evidence-based clinical resources."¹³ This system fuses the practices of CDS software with what is called black-box personalized medicine. Black-box medicine combines the use of big data and machine-learning algorithms to create predictive correlations.¹⁴ Doctors have recognized that because pa-

7. *10 Innovative Clinical Decision Support Programs*, INFORMATIONWEEK HEALTHCARE, <http://www.informationweek.com/healthcare/clinical-information-systems/10-innovative-clinical-decision-support-programs/d/d-id/1101834?> (last visited Dec. 14, 2016).

8. *Clinical Decision Support*, HEALTHCARE INFORMATION AND MANAGEMENT SYSTEMS SOCIETY, <http://www.himss.org/library/clinical-decision-support> (last visited Dec 14, 2016).

9. Michael Greenberg & M. Susan Ridgely, *Clinical Decision Support and Malpractice Risk*, 306 JAMA 90–91, 90-91 (2011), <http://jamanetwork.com/journals/jama/article-abstract/1104038> (last visited Dec 14, 2016).

10. *Id.*

11. Wolters Kluwer, *Product*, UPToDATE, <http://www.uptodate.com/home/product> (last visited Dec 16, 2016).

12. GRAND ROUND TABLE, A BIG DATA APPROACH TO CLINICAL DECISION SUPPORT, 2-3, 2014, http://www.grandroundtable.com/pdf/GrandRoundTable_ClinicalAssistant.pdf.

13. *Id.* at 3.

14. See W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J.L. & TECH. 419 (2015) (defining the concept of black-box medicine and how it has changed the healthcare landscape); see also Ruben Amarasingham et al., *Implementing Electronic Health Care Predictive Analytics: Considerations And Challenges*, 33 HEALTH AFF. 1148, 1148 (2014) (describing the use of big-data in healthcare through prediction technology).

tients are different from each other, tailored treatment is more likely to be effective. This type of CDS software is not as prevalent in hospitals yet because black-box algorithms need to be tested and validated, meaning only large providers have sufficient datasets available for use. The results of a machine-learning algorithm may be accurate given enough data; however, because a scientist is unlikely to understand what specific factors can alter an algorithm to what extent, clinicians currently do not implement algorithms through the use of black-box software outside of a few larger health-care providers.

Even though this type of CDS software is not prevalent in hospitals yet, these connections are likely “to yield new diagnostic tests and treatments and to enable individually tailored medical decisions.”¹⁵ Black-box algorithms can answer questions about how best to treat a particular patient or even diagnose a specific ailment.¹⁶ Most importantly, advanced and personalized CDS software can cut down healthcare costs in terms of both time and money, saving lives and ensuring effective resource allocation. As Congress has recognized in its passage of the 21st Century Cures Act, encouraging the use of CDS software and black-box algorithms is a necessary part of advancing the medical field; however, the Congressional method of incentivizing such innovation does the opposite while jeopardizing patient safety at the same time.

As will be discussed below, CDS software, while effective, can cause problems if used in a negligent manner or without adequate data. This policy rationale alone may suffice for why the FDA may want to regulate CDS software; however, even if it does not, there are also statutory obligations under which the FDA already has the authority to regulate such software. Section 321(h) defines a medical device as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is: . . . intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease.”¹⁷ According to the FDA, and under statutory analysis of the section above, CDS software falls under that definition and thus, under the FDA’s jurisdiction.¹⁸

In 1986, the House Subcommittee on Investigations and Oversight held hearings on the use of advanced computer systems in medical care. The

15. Roger A. Ford & W. Nicholson Price, *Privacy and Accountability in Black-Box Medicine*, 23 MICH. TELECOM. & TECH. L. REV. 1, 3 (2016).

16. See, e.g., Steven I. Sherman et al., *Augmenting pre-operative risk of recurrence stratification in differentiated thyroid carcinoma using machine learning and high dimensional transcriptional data from thyroid FNA*, 33 J. CLINICAL ONCOLOGY 6044 (2015) (reporting about a study successfully using machine learning to classify thyroid cancer tumors).

17. 21 U.S.C. § 321(h) (2012).

18. JOHN F. MURRAY, CDRH REGULATED SOFTWARE: AN INTRODUCTION, <http://www.fda.gov/downloads/Training/CDRHLearn/UCM209129.pdf> (last visited Dec 16, 2016).

FDA submitted an unsigned statement regarding its jurisdiction, noting that “[m]edical software products that are marketed separately from a computer (generally referred to as stand alone software) and used with a computer to form a system which operates as a medical device will be treated as a medical device.”¹⁹ In 1989, the FDA published a draft guidance document that explained how the FDA planned to determine whether a computer-based product is a medical device and how the FDA intended to regulate such devices.²⁰ That policy was withdrawn in 2005 when the FDA determined that the current structure of the policy was impractical and that its regulatory approach should focus on the harm the specific device poses to patients, regardless of whether the device uses software or not.²¹ The FDA realized that harm was a more accurate measure in determining what restrictions it should place on the development and use of a medical device. Determinations based on the type of device would not accurately determine what dangers the FDA needed to address with each device. Until recently, the Center for Devices and Radiological Health (CDRH), the offshoot of the FDA that focuses on medical devices, has addressed each situation on a case-by-case basis.²²

The FDA stated, as early as 1986 and into 2011, that treatment recommendation and support software fall into the category of medical devices.²³ 21 CFR 820, regulating the quality of software systems governed under ‘medical device,’ requires that all software meet minimum design and purchasing control standards, regardless of what the software’s device Class actually is.²⁴ Then, based on the use of the medical device, regulation for software as a medical device (SaMD) differs by class, as proposed in the figure below.²⁵

19. Vincent Brannigan, *The Regulation of Medical Expert Computer Software as a Device Under the Food, Drug, and Cosmetic Act*, 27 JURIMETRICS J. 370, 370 (1987).

20. *Id.*

21. *Id.*

22. *Id.*

23. *Id.*

24. 21 C.F.R. § 820. The FDA uses a tiered, Class system to determine what level of regulation is necessary for any particular device. There are three Classes, with Class 1 referring to devices that do not need much regulatory oversight (e.g., Band-Aids) and Class 3 referring to devices that need much more oversight (e.g., robot-assisted surgical devices).

25. *Software as a Medical Device (SaMD): Clinical Evaluation*, Food & Drug Admin. (2016), <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM524904.pdf>.

Not SaMD	SaMD Categories								Not SaMD	
Retrieves Information	I			II			III		IV	Software used in Closed Loop Interventions
Organizes Data	Informs Non-Serious	Informs Serious	Drives Serious	Informs Critical	Drives Serious	Treats/Diagnoses Non Serious	Drives Critical	Treats/Diagnoses Serious	Treats/Diagnoses Critical	
Optimizes Processes										

FIGURE 1. CATEGORIES OF SOFTWARE AS MEDICAL DEVICES

Some commentators have argued that the function of CDS software is “to support the clinical judgment of a healthcare professional, not to replace it,” and therefore it should not be regulated by the FDA. The FDA caused even more confusion by saying that they would regulate high-risk CDS but not low-risk software, without providing any indication of what would constitute high or low risk.²⁶ The CDS coalition, a group of CDS developers and manufacturers, recently released a white paper asking the FDA to clarify the scope of CDS regulation and the requirements of any such regulation.²⁷ The paper stated that “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.”²⁸ In the past, CDS developers have run into problems deciding what class their software falls into or at the least, what class the FDA will choose for their software. For that reason, CDS developers have asked for clarification for many years; however, the FDA has generally only given vague guidance documents about the regulation of CDS software. As a response to some of this confusion regarding what the FDA does or does not regulate, Congress passed the 21st Century Cures Act, entirely changing the FDA’s jurisdiction over medical software.

II. THE 21ST CENTURY CURES ACT AND THE DEREGULATION OF CLINICAL DECISION SUPPORT SOFTWARE

On December 13, 2016, President Obama signed into law the 21st Century Cures Act, which Congress passed with overwhelming support.²⁹ The stated purpose of the Act was to “advance medical product innovation and

26. Greg Slabodkin, *21st Century Cures Act clarifies FDA regulation of software*, HEALTHDATA MANAGEMENT (2016) <http://www.healthdatamanagement.com/news/21st-century-cures-act-clarifies-fda-regulation-of-software> (last visited Dec 5, 2016).

27. CLINICAL DECISION SUPPORT COALITION, *WEIGHING THE IMPACT OF FDA REGULATORY UNCERTAINTY ON CLINICAL DECISION SUPPORT DEVELOPMENT 1–2* (2016), <http://cdscoalition.org/wp-content/uploads/2016/02/CDS-Survey-White-Paper-Final-2016.pdf>.

28. *Id.* at 6.

29. Katie Reilly, *President Obama Signs the 21st Century Cures Act*, TIME (Dec. 13, 2016), <http://time.com/4599295/president-obama-cures-act-livestream-online/>.

ensure that patients get access to treatments as quickly as possible, with continued assurance from high quality evidence that they are safe and effective.”³⁰ The Act addressed many of the trickier issues the FDA dealt with in the last few years, including how to regulate medical software that qualifies as a medical device.³¹ The Act removed five categories of software from the definition of medical device, and thus from the FDA’s jurisdiction. Specifically § 3060(a) states that:

[T]he Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j) is amended by adding at the end the following:

The term device, as defined in section 201(h), shall not include a software functioning that is intended – . . . for the purpose of – (i) displaying, analyzing, or printing medical information about a patient or other medical information (such as peer reviewed clinical studies and clinical practice guidelines); (ii) SUPPORTING OR PROVIDING RECOMMENDATIONS TO A HEALTH CARE PROFESSIONAL ABOUT PREVENTION, DIAGNOSIS, OR TREATMENT OF A DISEASE OR CONDITION; AND (iii) 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 such recommendation to make a clinical diagnosis or treatment decision regarding an individual patient.³²

Under this provision, the FDA will not regulate software using big data or clinical-trial aggregation to provide clinical decision support to healthcare professionals if such software allows health professionals to independently review the basis.³³ Although, some FDA policies have already exempted portions of software (although not explicitly CDS) from regulation, the above language codifies limitations on enforcement to some degree.³⁴

To be clear, this section does have a few exceptions as it allows for some level of FDA guidance and regulation. First, image analysis software and *in vitro* diagnostic software will continue to fall under the definition of ‘medical device,’ and the FDA will continue to have full jurisdiction over

30. Robert M. Califf, *21st Century Cures Act: Making Progress on Shared Goals for Patients*, FDA VOICE, Dec. 13, 2016, <https://blogs.fda.gov/fdavoices/index.php/2016/12/21st-century-cures-act-making-progress-on-shared-goals-for-patients/>.

31. Sarah Faulkner, *How the 21st Century Cures Act Will Affect Medical Devices*, MASSDEVICE (Dec. 8, 2016), <http://www.massdevice.com/21st-century-cures-act-will-affect-medical-devices/>.

32. 21st Century Cures Act § 3060(a) (emphasis added).

33. *See id.*

34. Michele L. Buenafe & M. Elizabeth Bierman, *21st Century Cures Act and Its Effect on Digital Health*, NAT’L L. REV. (Dec. 9, 2016), <http://www.natlawreview.com/article/21st-century-cures-act-and-its-effect-digital-health> (last visited Dec. 11, 2016).

those softwares.³⁵ Second, CDS software may still be considered a ‘medical device’ if it “would be reasonably likely to have serious adverse health consequences.”³⁶ For any software that is likely to have serious consequences, developers may still have to refer to past FDA enforcement decisions and discretionary policy to understand the scope and effect of regulation.³⁷

III. THE COSTS OF DEREGULATION: THE IMPACT ON PUBLIC SAFETY AND INCENTIVES FOR INNOVATION

A. *Lack of Regulation as a Public Health Concern*

The 21st Century Cures Act, while attempting to loosen regulation on software, has overlooked many of the reasons the FDA may have regulated software as a medical device. There are two major public health issues with the unregulated use of CDS, especially CDS software that is dependent on big data and black-box algorithms. This section on public health and safety concerns will first consider the CDS issue of ‘alert fatigue’ and then the issue of algorithm validation.

Basic types of clinical decision support software, such as those tied to prescription-related concerns, use automated warnings to alert clinicians about possible complications. These complications can arise as possible drug interactions with other drugs or can be specific to a patient’s individual allergies or dosage issues. However, multiple studies show that CDS software may often cause more human error through an overabundance of alerts—a concept known as alert fatigue.³⁸ Because many CDS developers over-include which warnings a system will automatically generate, physicians using the system have a high rate of “alert fatigue, . . . undermin[ing] the utility the systems offer.”³⁹ For example, some systems trigger a “medication interaction alert” when one of the prescriptions is a topical salve a nurse should apply but could be problematic if the patient ingested the drug in large amounts.⁴⁰ Because of these type of warnings—warnings that are

35. 21st Century Cures Act § 3060(a)(1).

36. *Id.* at § 3060(a)(3)(A).

37. *See id.* (meaning FDA guidance will also be necessary to understand what constitutes a reasonable likelihood of ‘serious adverse health consequences.’).

38. Michael Greenberg & M. Susan Ridgely, *Clinical Decision Support and Malpractice Risk*, 306 J. AM. MED. ASS’N 90–91 (2011), <http://jamanetwork.com/journals/jama/article-abstract/1104038> (last visited Dec. 14, 2016).

39. *Id.*

40. Aaron S Kesselheim et al., *Clinical Decision Support Systems Could Be Modified To Reduce ‘Alert Fatigue’ While Still Minimizing The Risk Of Litigation*, 30 HEALTH AFF. 2310 (2011) (citing Gilad J. Kuperman et al., *Medication-related Clinical Decision Support in Computerized Provider Order Entry Systems: A Review*, 14 J. AM. MED. INFORMATICS ASS’N 29 (2007)).

less than useful—physicians ignore 49-96 percent of all alerts.⁴¹ Studies show that physicians consistently miss or ignore useful alerts, studies that have been confirmed by this author’s personal research with individual practitioners regarding the rate at which they read CDS alerts versus what they ignore.⁴²

Without regulation from the FDA, there are no requirements for what kind of alerts and how many alerts a specific CDS system should use. Software creators are worried about liability; without guidance on what alerts are actually helpful, creators are more inclined to just include every warning possible without regard for its utility. FDA requirements might help set a standard for what type of alerts are helpful and necessary. There is also no metric to determine whether software is more harmful to patients when alert fatigue is taken into account. Alert fatigue is not just a problem for basic CDS software that serves as an electronic overlay on electronic medical record systems. If a physician ignores CDS software without a meritorious reason, a patient may be at risk regardless of which type of software is being used.

Unlike alert fatigue, the second public health concern with deregulating CDS software concerns the effects of black-box medicine and use of algorithms that may contain a large number of computations and correlations that are not decipherable by any one group of clinicians. These algorithmic, predictive relationships must be validated by software developers to assure that clinicians use them safely and effectively.⁴³ When the software compares a “deidentified” patient’s data to evidence from clinical trials, studies, and more, there are a multitude of issues that one cannot account for, issues involving the individualized reactions of the patient, whether the patient followed the treatment plan, and even what other medications a patient may be taking. The doctor who enters the patient’s data could introduce human error through incorrect inputs. That issue is not as concerning since there are ways to ensure data is entered correctly.

The larger concern, as mentioned above, is how to validate black-box algorithms, especially when the algorithms are not based on just one or two moving variables, but instead require a computer to analyze tens, hundreds, or thousands of variables of unequal value. Although the Cures Act does not directly change governance of black-box algorithms because it applies to

41. *Id.* (citing Heleen van der Sijs et al., *Overriding of Drug Safety Alerts in Computerized Physical Order Entry*, 13 J. AM. MED. INFORMATICS ASS’N 138 (2006), <http://jamia.oxfordjournals.org/content/jaminfo/13/2/138.full.pdf> (last visited Dec. 17, 2016)).

42. *See* Interview with Easha Patel, Virginia Commonwealth University (2016) (Regarding the use of CDS in OB/GYN practice) (on file with author); *see also* Interview with Vandan Patel, University of Michigan (Regarding the use of CDS in orthopedic surgery practice) (on file with author); *See generally*, ROBERT WACHTER, *THE DIGITAL DOCTOR* (2015).

43. W. Nicholson Price II, *Big Data, Patents, and the Future of Medicine*, 37 CARDOZO L. REV. 1401, 1416 (2016).

technology where a healthcare professional can independently review conclusions, the technology is quickly moving to that point. These algorithms are called black-box algorithms specifically because the mechanisms and bases for each decision may not be visible or even comprehensible to human scientists. These algorithms are difficult to implement in an evidence-based medical community without more information about how each algorithm works or some independent guarantee that the algorithm is truly effective.

Not validating black-box algorithms can be problematic for two reasons.⁴⁴ First, without validation, clinicians are not likely to trust the algorithm and therefore not likely to use it, undermining incentives for innovation. Second, although regulatory approval might signal validation to clinicians even though they do not understand the algorithm themselves, without some method of validation, regulating black-box algorithms becomes difficult. Without regulation, there is no assurance of high quality, making the algorithm unsafe for public use making it hazardous for clinicians who are concerned about liability to rely on it. While there may be private oversight, it can be difficult to coordinate considering how different healthcare systems use different software and have varying standards. The creation of information about new medical technologies is itself a form of innovation that must be protected through validation.⁴⁵ As discussed in Part IV, while there are other methods of validation outside of regulation, regulatory schemes often provide a stamp of approval while also aggregating information that other forms of validation cannot.

B. *Lack of Regulation as an Innovation Concern*

While public health concerns surrounding CDS deregulation affect clinicians, and patients alike, firms are also impacted by deregulation. At first glance, deregulation of CDS software and black-box algorithms may seem to open up the field of software and algorithms free of the burdens of regulation. A decrease in regulation is often cited as a factor in increasing innovation; however, that may not be correct with regard to software and algorithms for advanced healthcare. Black-box medicine and even basic prescription-based CDS software require substantial investments from firms.⁴⁶ Without regulation or intellectual property protection, there is a lack of adequate incentive for firms to continue developing this kind of software, especially when costs are likely to continue rising.⁴⁷

44. *Id.* at 1416 n.70.

45. *Id.* at 1416 n. 71 (citing Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007)).

46. *Id.* at 1408.

47. *Id.* at 1418 (stating that “[d]atabases, algorithms, and the knowledge that algorithms are reliable are all information goods, which are difficult to keep exclusive once known. Accordingly, intellectual property—or a substitute incentive set—is likely necessary for its socially optimal development.”).

With the 21st Century Cures Act, regulation and regulatory exclusivity, the only avenues available for full-fledged protection of CDS software (basic and black-box), are now gone.⁴⁸ Patent exclusivity, as opposed to regulation and regulatory exclusivity from the FDA, also does not exist for CDS software and black-box algorithms. After the Supreme Court's decision in *Prometheus* in 2012, patents are no longer a valid option to protect the intellectual property behind algorithms based on diagnostic models.⁴⁹ Black-box algorithms and prescription suggestions arguably describe natural laws and "tell[] doctors to engage in well-understood, routine, conventional activity."⁵⁰ *Prometheus* removed patent protection for a majority of medical diagnostic software and for similar innovations in the future, such as black-box medicine, by entirely removing the technology from subject-matter eligibility. Even if subject-matter eligibility was not an issue, § 112's requirements regarding enablement and written description also limit the patentability of black-box algorithms (although those concerns may not be as pervasive with the current, prescription-based CDS software). As will be discussed in Part IV, regulatory exclusivity through FDA jurisdiction over CDS and black-box algorithms is the ideal way to provide protection for software developers and incentivize innovation. In fact, a lack of protections is quite likely to decrease innovation in the long run.

IV. FDA REGULATION OF SOFTWARE: INCENTIVIZING INNOVATION AND PROVIDING CONFIDENCE

A. Regulation to Address Public Health and Safety Concerns

Although the 21st Century Cures Act removes CDS software from the FDA's statutory jurisdiction, Part III acknowledges why this is a mistake. Without regulation, clinicians are less likely to use CDS and black-box algorithms, algorithms are not likely to be validated, and firms are unlikely to continue developing algorithms without some level of incentive. FDA regulation through minimum safety standards for CDS software and a regime of regulatory exclusivity would be a better option to address public health concerns and ensure ongoing innovation.

Proponents of the 21st Century Cures Act argue that any public health concerns are adequately addressed through an 'escape hatch' in the act, stating that the FDA may retain jurisdiction over software "reasonably likely to

48. While this paper only briefly talks about the lack of intellectual property incentives, some authors have suggested trade secrecy may be a better option. For a discussion on why trade secrecy specifically fails in the CDS and black-box algorithm field, see W. Nicholson Price II, *Patents, Big Data, and the Future of Medicine*, 37 *CARDOZO L. REV.* 1401, 1433 (2016) (discussing how secrecy limits the value of black-box algorithms, which depends on sharing information with others).

49. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 566 U.S. 66, 92 (2012).

50. *Id.* at 79.

have serious adverse health consequences.”⁵¹ There are two problems with this reading of the statute. First, there is no definition of what constitutes a ‘serious adverse health consequence,’ which continues to leave software developers in limbo regarding what level of FDA regulation firms should expect when developing software. Without further guidance, the escape hatch is vague and creates less incentive to learn about the health consequences of the software. Software developers are less likely to actively learn about the health consequences of their software because knowing the consequences would require disclosing the consequences, lengthening the approval process. Furthermore, the purpose of regulation requires the FDA to determine what technology is likely to have adverse health consequences. Without more regulation, however, the FDA is not likely to learn which technologies would fall under such a label, because such information would largely come from requiring companies to submit studies for approval.

Second, the escape hatch actually requires so much administrative change that it is not likely to be effective in a timely manner. The escape-hatch provision actually states that to bring software back under FDA regulation,

[T]he agency must ISSUE A FINAL ORDER IN THE FEDERAL REGISTER providing its rationale based upon the potential for and severity of patient harm if the software does not perform as intended, the extent to which the software is intended to support the judgment of a healthcare professional, whether a healthcare professional has a reasonable opportunity to review the basis of the information or treatment recommendation provided, and the intended user and use environment.⁵²

In order for the requisite changes to take place, the FDA will have to go through a notice and comment procedure to reregulate certain types of software, a process that could take at minimum a few months and is more likely to actually take a few years.

Instead of dancing between regulating and not regulating CDS software, it would be better if the FDA did regulate the software but ensured that the regulations were tailored to carefully considered public safety issues and providing temporary exclusivity for developers. A trade-off between regulation and exclusivity has worked well for the FDA in the past and would be

51. 21st Century Cures Act § 3060.

52. Jeffrey K. Shapiro & Jennifer D. Newberger, *Highlights of Medical Device Related Provision in the 21st Century Cures Act*, FDA LAW BLOG (Dec. 8, 2016), <http://www.fdalaw-blog.net/2016/12/highlights-of-medical-device-related-provision-in-the-21st-century-cures-act/>; see also *id.*

ideal in the CDS context.⁵³ Some clinicians worried about the public health issues noted in Part III are already asking for more oversight, suggesting that FDA involvement could “help reduce any real or perceived liability on the part of vendors, purchasers, and users.”⁵⁴ According to this same group of physicians, “oversight can help protect patients by ensuring that systems are of high quality and include approved parsimonious and tailored decision support.”⁵⁵

As mentioned above in Part III, alert fatigue is an important patient safety concern that is not likely to be addressed without regulatory oversight. The FDA is best positioned to address issues relating to patient safety, especially when such issues are a direct result of software constituting a medical device. A transnational example of a decrease in alert fatigue demonstrates why. England’s Department of Health has already developed software design standards, including clinical decision support system standard, that are mandatory for all software suppliers.⁵⁶ While these standards are not stringent to ensure malleability, the minimal standards ensure that patient protection is at the forefront of developing CDS software.⁵⁷

The FDA also has the regulatory structure to ensure that developers and firms train clinicians how to use CDS software in a safe manner. Oversight of manufacturer trainings, which has already worked in the past, is the best way to ensure alert fatigue does not occur. The FDA already has the infrastructure to conduct such trainings since it does so with other medical devices; furthermore, it has the proper incentives to continue the program, incentives that are not motivated by profit. User training can ensure that physicians do not unreasonably ignore alerts.⁵⁸ Currently, there is inadequate communication of system limitations and user error issues to physicians, the individuals who depend on CDS software in making concrete recommendations. Removing FDA jurisdiction over CDS software and black-box algorithms will only decrease any incentive to train users. This sort of FDA oversight would not require anything more than what the FDA already does with regard to device manufacturers. The FDA already mandates that device companies establish procedures to identify training needs

53. Yaniv Heled, *Regulatory Competitive Shelters*, 76 OHIO ST. L.J. 299, 327-29 (2015) (listing multiple regimes of regulatory exclusivity, thirteen of which the FDA administers to promote innovation).

54. Aaron S. Kesselheim et al., *Clinical Decision Support Systems Could Be Modified To Reduce ‘Alert Fatigue’ While Still Minimizing The Risk Of Litigation*, 30 HEALTH AFF. 2310, 2311 (2011).

55. *Id.* at 2314.

56. *Id.* (citing *Health Informatics - Application of clinical risk management to the manufacture of health software*, NAT’L Health SERV. CONNECTING FOR HEALTH (Apr. 2009), <https://web.archive.org/web/20130415060854/www.connectingforhealth.nhs.uk/systemsandservices/clinsafety/dscn/dscn14.pdf>).

57. *See id.*

58. *Id.*

and ensure personnel are appropriately trained to perform their assigned tasks.⁵⁹ The training must already be documented in records that can be made available to FDA investigators upon request.⁶⁰

B. Regulation to Address Diminishing Incentives to Innovate

As mentioned in Part III, another issue with deregulating CDS software is that deregulation diminishes developers' incentives to innovate in two ways. First, regulation creates a demand for information that motivates information production, which is a form of innovation. The second is that regulatory approval enhances demand for a new technology, which makes it more profitable, and thus stimulates innovation. Similar to past actions by the FDA, regulatory exclusivity provides incentives better tailored to software and algorithms than other, traditional methods of intellectual property protection. The FDA would be the right agency to limit pre-market approval of algorithms and software to competitors.⁶¹ Setting up a pre-market approval regime would not only incentivize development, it would provide a method to ensure implementation of the above-mentioned safety standards before software reached the market.

Regulatory exclusivity for predictive clinical software would not be significantly different from existing preapproval regimes the FDA already has in place.⁶² The FDA could withhold approving imitator products to market and distribute similar software for a set amount of years.⁶³ This withholding would serve as a reward to the firm that initially invents the software while encouraging competitors to make significant, positive changes to the software either while waiting to gain approval or to make a completely new product that would separately qualify for regulatory approval. Unlike regulatory exclusivity periods for biologics, which last for four years of market exclusivity and an additional eight years of data exclusivity,⁶⁴ or even generic drugs, which last for five years,⁶⁵ a two or three year term of exclusivity would probably suffice for CDS software. Software is constantly

59. 21 C.F.R. § 820.25(b).

60. See Marie Dorat, *Training and the FDA – What do They Require?*, 360 FACTORS (last visited Dec. 18, 2016) <http://www.360factors.com/blog/training-and-the-fda-what-do-they-require/>.

61. See W. Nicholson Price II, *Patents, Big Data, and the Future of Medicine*, 37 CARDOZO L. REV. 1401 (2016).

62. Yaniv Heled, *Regulatory Competitive Shelters*, 76 OHIO ST. L.J. 299, 302 (2015).

63. The author acknowledges that terms like “similar software” and “imitator products” are loose terms that will also create uncertainty. The current suggestion is to preclude immediate approval of any other software that generates identical recommended courses of treatment; however, firms could easily circumvent this by relying on a different algorithm.

64. See 42 U.S.C. § 262(k)(7) (2012) (granting four years of market exclusivity and an additional eight years of data exclusivity to biologics).

65. See 21 U.S.C. § 355(j)(5)(F)(ii) (2012) (granting five years of market exclusivity for new chemical entities).

changing so long-term exclusivity would not be as beneficial here. Furthermore, once a hospital system adopts a specific software system for clinical use, the hospital system is unlikely to immediately change to another software system after two to three years. Constant changes would require hospitals to increase spending on a new product, increase costs for installation, and also require new trainings for physicians. There is a built-in presumption that once a hospital buys a set of software products, they will continue using that same system for as long as possible, especially if the system comes with updates, as most CDS software does.⁶⁶

Regulatory exclusivity would also be more flexible than any changes to the patent process, which would require a drastic amount of work and would not just affect software patents but all patentable subject matter.⁶⁷ The FDA, due to its mandate to protect innovation and the health and safety of patients, would also have more experience with the specific technology behind CDS software and black-box algorithms.⁶⁸ Due to the FDA's regulation of medical software as a medical device since the late 1980's, the FDA is already aware of the discrepancies noted in Part III regarding validation of software and black-box medicine algorithms. The FDA's Sentinel database is evidence of the FDA's institutional knowledge regarding big data management and the issues with validating any assumptions made through the use of such data. For 25 years now, the FDA has issued guidelines and regulations regarding software as medical devices.⁶⁹ Regulatory exclusivity, which would require software developers to hand over treatment algorithms to the FDA and show the basis for why the developer believes the algorithm is valid, would provide more of a check on validation than complete deregulation would. Creating stronger guidelines and mechanisms for clinical validation of algorithms, as opposed to no guidelines at all, would allow for clinical validation, faith in the use of medical software and algorithms, and effective innovation instead of innovation for the sake of innovation.

The only issue with regulatory exclusivity is one that the Court already suggested through its holding in *Prometheus*. If regulatory exclusivity prevents other firms from relying on 'natural' laws to create medical software, that sort of exclusivity could possibly decrease innovation by others; however, the use of regulatory exclusivity by the FDA with regards to biologics and generics shows that a temporary period of exclusivity has only increased incentives to innovate, not decreased such incentives. While this solution is

66. The author notes that this suggests that a first-mover advantage may be enough to capture the market, making regulatory exclusivity unnecessary. While that may be true, regulatory exclusivity also provides more confidence from investors in the market because it allows a legal assertion of rights that a first-move may not always be able to access.

67. Price II, *supra* note 61, at 1446-47.

68. U.S. FOOD & DRUG ADMINISTRATION, FDA MISSION, <http://www.fda.gov/AboutFDA/WhatWeDo/> (last visited Dec. 18, 2016).

69. See Murray, *supra* note 18.

not perfect, it is better to protect innovation and patient safety than the deregulation proposed by the 21st Century Cures Act.

CONCLUSION

Contrary to the purposes behind Congressional passage of the 21st Century Cures Act, removing FDA jurisdiction over CDS software and black-box algorithms is unlikely to incentivize innovation. Regulatory exclusivity grants from the FDA to innovative software developers would actually incentivize innovation. Moreover, pre-approval regimes would ensure clinicians and physicians who use CDS software and black-box algorithms are adequately trained and are only using software that has been validated with sound, scientific principles. Medical software is critical to advancing healthcare and providing the best possible patient outcomes. At least with regard to the current state of medical software, the FDA is best equipped to ensure safety and innovation in the field.