June 28, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Submitted electronically via http://www.regulations.gov

RE: Development of 21st Century Cures Act Section 3060 Required Report: Request for Input (FDA-2018-N-1910)

AMIA is pleased to provide input that will inform the U.S. Food and Drug Administration's (FDA) current thinking on benefits and risks to health associated with the software functions excluded from the device definition by the Cures Act.

AMIA is the professional home for more than 5,500 informatics professionals, representing front-line clinicians, researchers, educators and public health experts who bring meaning to data, manage information and generate new knowledge across the health and health care enterprise. As the voice of the nation's biomedical and health informatics professionals, AMIA plays a leading role in advancing health and wellness by moving basic research findings from bench to bedside, and evaluating interventions, innovations, and public policy across settings and patient populations.

As we understand it, FDA is looking for input on benefits and risks to health associated with the software functions excluded from the device definition by the Cures Act. The software functions excluded from the definition of device under section 3060 of Cures are:

- For administrative support of a healthcare facility;
- For maintaining or encouraging a healthy lifestyle;
- To serve as electronic patient records;
- For transferring, storing, converting formats, or displaying data; or
- To provide limited clinical decision support.

AMIA and the informatics community have been central to the study of "health IT as an intervention." While the use of IT and software for facilitation of communication is well understood, the evaluation of this facilitation in support of a healthy lifestyle or decision aid is less so. Leading experts who study the intersection of health IT and care delivery note that the safety and safe use of health IT must be viewed through a socio-technical model to understand and improve health IT applications at various stages of development and implementation.[1] To view health IT as

[1] Sittig D, Singh H. A New Socio-technical Model for Studying Health Information Technology in Complex Adaptive Healthcare Systems. Qual Saf Health Care. 2010 Oct; 19(Suppl 3): i68–i74. doi: 10.1136/qshc.2010.042085

an intervention acknowledges that the context (when, why, and how) of its use can impact health outcomes, and suggests that there ought to be normative principles for how to leverage health IT to optimize patient care.[2]

Enclosed in Table 1, we have developed a preliminary review of relevant research into the specific benefits and risks to health associated with each of the software functions excluded by Cures. While not exhaustive, the evidence to-date suggests a wide array of potential benefits as well as an assortment of emerging risks to personal health and safety. We have categorized the research according to the five functions excluded from the definition of a device as follows:

- **Administrative**: For administrative support of a healthcare facility;
- **mHealth**: For maintaining or encouraging a healthy lifestyle;
- **EHR/PHR**: To serve as electronic patient records;
- **MDDS**: For transferring, storing, converting formats, or displaying data; and
- **CDS**: To provide limited clinical decision support.

Our summary of evidence focuses on mHealth, EHR/PHR, and CDS functionalities.

As the FDA endeavors to better understand this space, AMIA offers its support and the support of its members with long-standing expertise in assessing outcomes related to the use of such software functionalities. Should you have questions about these comments or require additional information, please contact Jeffery Smith, Vice President of Public Policy at jsmith@amia.org or (301) 657-1291. We look forward to continued partnership and dialogue.

Sincerely,

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(Enclosed: Annotated Bibliography of Evidence Exploring Risks and Benefits of Certain Software Functionalities)

[2] Bates DW, Kuperman GJ, Wang S, et al. Ten Commandments for Effective Clinical Decision Support: Making the Practice of Evidence-based Medicine a Reality. J Am Med Inform Assoc. 2003 Nov-Dec; 10(6): 523–530.

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The introduction of health IT applications to healthcare delivery has unambiguously improved patient safety and saved lives.[3,4] Findings from a 2014 literature review demonstrated benefits in medication safety and dosing, increased adherence to clinical guidelines and protocols (including screenings and vaccinations), and the efficiency of care. [5] For example, a 2015 systematic review of how mHealth tools support chronic disease management found a significant improvement in adherence and behaviors for 56 percent of RCT studies, and 39 percent of RCT studies showed improvement in disease-specific clinical outcomes.[6] However, health IT has also introduced new, novel, and complex threats to patient safety.

Evidence gathered through experience in the last several years of health IT adoption by hospitals and physicians confirms that software design, implementation decisions, user training, and maintenance processes can all have a material impact on the safety of health IT. From 2010 to 2013, 120 health IT-related Sentinel Events (SEs) – an event that has resulted in an unanticipated death or major permanent loss of function – were reported to the Joint Commission.[7] Further, the *Journal of Patient Safety* reviewed a medical malpractice claims database from 2012 to 2013 and found that while less than one percent of claims involved health IT, a total of 248 cases demonstrated that "Adverse events associated with health IT vulnerabilities can cause extensive harm and are encountered across the continuum of health care settings and sociotechnical factors."[8] Lastly, a recent spate of high-profile ransomware attacks involving twelve hospitals' EHR data has added a new dimension of concern for those focused on health IT safety: without access to digital information, clinicians are "flying blind," causing patients to be relocated and high-risk surgeries to be cancelled.[9] In all instances, experts believe reported problems represent a small fraction of the total number of adverse events that go unreported and unanalyzed. Please see below, in Table 1, a listing of relevant research related to the subject of benefits and risks to health posed by select categories of software functionalities excluded from the definition of device in Cures.

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[3] Levine DM, Healey MJ, Wright A, et al. Changes in the quality of care during progress from stage 1 to stage 2 of Meaningful Use, Journal of the American Medical Informatics Association, Volume 24, Issue 2, 1 March 2017, Pages 394–397, https://doi.org/10.1093/jamia/ocw127

[4] Furukawa MF, Spector WD, Limcangco MR et al. Meaningful use of health information technology and declines in in-hospital adverse drug events, Journal of the American Medical Informatics Association, Volume 24, Issue 4, 1 July 2017, Pages 729–736, https://doi.org/10.1093/jamia/ocw183

[5] Jones SS Rudin RS Perry T Shekelle PG. Health information technology: an updated systematic review with a focus on meaningful use. Ann Intern Med. 2014;160(1):48–54.

[6] Hamine S, Gerth-Guyette E, Faulz D, et al. Impact of mHealth Chronic Disease Management on Treatment Adherence and Patient Outcomes: A Systematic Review J Med Internet Res. 2015 Feb; 17(2): e52.

[7] Castro G. Investigations of Health IT-related Deaths, Serious Injuries, or Unsafe Conditions. ONC Health IT Safety Webinar Series. Beginning slide 23. http://www.healthitsafety.org/uploads/4/3/6/4/43647387/webinar_1_full_deck_2014-12-18_v5.pptx. 2014.

[8] Gruber et al

[9] Simonite, T., "With Hospital Ransomware Infections, the Patients Are at Risk," *MIT Technology Review*. April 1, 2016

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Table 1: Annotated Bibliography of Evidence Exploring Risks and Benefits of Certain Software Functionalities

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
2015	Impact of mHealth Chronic Disease Management on Treatment Adherence and Patient Outcomes: A Systematic Review	Hamine, Saee, Emily Gerth-Guyette, Dunia Faulx, Beverly B. Green, and Amy Sarah Ginsburg.	*Journal of Medical Internet Research*	Study does not address risks	Review suggests a significant improvement in adherence and behaviors for 56% of RCT studies. 39% of RCT studies showed improvement in disease specific clinical outcomes	This systematic literature review (1980-2014) evaluated the effectiveness of mHealth in supporting chronic disease management. Of the 107 studies, 27 were RCTs.	mHealth
2018	Prescribable mHealth apps identified from an overview of systematic reviews	Byambasuren, Oyungerel, Sharon Sanders, Elaine Beller, and Paul Glasziou	*npj Digital Medicine*	Low evidence of effectiveness		This systematic literature review (2008-2018) evaluated RCTs of stand-alone mHealth apps. The review included 6 systematic reviews of 23 RCTs evaluating 22 apps. Most trials used a small sample size, short duration, and had a high risk of bias. This manuscript points out the need for more rigorous research is needed in this area.	mHealth
2015	Low Quality of Free Coaching Apps With Respect to the American College of Sports Medicine Guidelines: A Review of Current Mobile Apps	Modave, F., Bian, J., Leavitt, T., Bromwell, J., Harris III, C., & Vincent, H.	*JMIR mHealth and uHealth*	The apps are not evidence based. There is also risk of use by patients who do not possess needed awareness of safety and risks of injury.		This is a systematic assessment of the quality of mHealth fitness apps. This assessment of 30 free mHealth apps found that very few apps were evidence based and a gap in knowledge about safe use when starting a physical routine program.	mHealth
2018	Trends in user ratings and reviews of a popular yet inaccurate blood pressure-	Plante, Timothy B., Anna C. O'Kelly, Zane T. Macfarlane, Bruno Urrea, Lawrence J.	*Journal of the American Medical Informatics Association*	Consumers risk making inaccurate decisions about diet and exercise based on inaccurate blood		This article is an analysis of user ratings of an inaccurate, unregulated blood pressure measurement device. Authors found that despite the device's inaccuracy, users perceived the app to be accurate and posted high user reviews. This illustrates a	mHealth

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
	measuring smartphone app	Appel, Edgar R. Miller III, Roger S. Blumenthal, and Seth S. Martin		pressure readings.		general lack of awareness of accuracy, evidence, and safety of mHealth app consumers.	
2015	Using Health Information Technology to Support Quality Improvement in Primary Care	Higgins TC, Crosson J, Peikes D, et al.	AHRQ White Paper		HIT improves care quality and patient outcomes in primary care settings.	The effective use of health information technology (IT) by primary care practices to facilitate quality improvement (QI) can help practices improve their ability to deliver high quality care and improve patient outcomes.	EHR/PHR
2015	Recent Evidence that Health IT Improves Patient Safety	Banger A, Graber ML.	ONC Issue Brief prepared by RTI International		Health IT improves care quality and patient safety.	This brief includes recent systematic reviews on the topic.	EHR/PHR
2017	Medication Errors Attributed to Health Information Technology	Lawes S, Grissinger M	Pennsylvania Patient Safety Advisory	Medication errors		Drawing from 889 medication error reports submitted over a 6-month period, this analysis found that more than half of the recorded incidents were associated with computerized provider order entry.	EHR/PHR

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
2012	Health IT and Patient Safety: Building Safer Systems for Better Care	Committee on Patient Safety and Health Information Technology	Institute of Medicine study		Care quality and patient safety.	This is a consensus study report by IOM.	EHR/PHR
2012	Quality Measurement Enabled by Health IT: Overview, Possibilities, and Challenges	Anderson KM, Marsh CA, Flemming AC, et al.	AHRQ environmental snapshot prepared by Booz Allen Hamilton		Care quality	Elaborates how health IT can be utilized to measure and improve care quality and existing challenges.	EHR/PHR
2015	Reducing diagnostic errors in primary care. A systematic meta-review of computerized diagnostic decision support systems by the LINNEAUS collaboration on patient safety in primary care.	Martine Nurek, Olga Kostopoulou, Brendan C Delaney & Aneez Esmail	*European Journal of General Practice*		Reduces diagnostic errors	Systematic review that shows developing a CDDSS that is able to utilize dynamic vocabulary tools to quickly capture and code relevant diagnostic findings, and coupling these with individualized diagnostic suggestions based on the best-available evidence has the potential to improve diagnostic accuracy, but requires evaluation.	CDS

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
2014	Clinical Decision Support: Effectiveness in Improving Quality Processes and Clinical Outcomes and Factors That May Influence Success	Murphy EV	*Yale Journal of Biology and Medicine*		Improves care quality and clinical outcomes	Provides evidence on the effectiveness of CDS.	CDS
2011	Impact of Electronic Health Record Clinical Decision Support on Diabetes Care: A Randomized Trial.	O'Connor PJ, Sperl-Hillen JM, Rush WA, et al.	*Annals of Family Medicine*		Improves type 2 diabetes management	This study is a specific example of benefits of CDS in type 2 diabetes with a randomized trial. The sample included 11 clinics with 41 consenting primary care physicians and the physicians' 2,556 patients.	CDS
2012	Enabling Health Care Decision making Through Clinical Decision Support and Knowledge Management.	Lobach D, Sanders GD, Bright TJ, et al	*Evidence Report/Technology Assessment*		CDSSs/KMSs are effective in improving health care process measures across diverse settings using both commercially and locally developed systems	Meta-analysis publications in between 1976 to 2010.	CDS

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
2013	Integrating Clinical Decision Support Tools into Ambulatory Care Workflows for Improved Outcomes and Patient Safety	Hummel J	ONC grant report		Improved outcomes and patient safety.	Shows effects of CDS in the ambulatory care setting.	CDS
2012	Computerised decision support systems for healthcare professionals: an interpretative review	Cresswell K, Majeed A, Bates DW, et al	*Informatics in Primary Care*	Data inaccuracy and disruption of clinical workflows.	Care quality and patient safety	This paper provides systematic evidence on the benefits and risks of CDS in care quality and patient safety.	CDS
2008	Grand challenges in clinical decision support	Sittig DF, Wright A, Osheroff JA, Middleton B, Teich JM, Ash JS, Campbell E, Bates DW.	*Journal of Biomedical Informatics*			Using an iterative, consensus-building process, the study identified a rank-ordered list of the top 10 grand challenges in clinical decision support. This list was created to educate and inspire researchers, developers, funders, and policy-makers. The challenges can be utilized to evaluate new CDS software.	CDS

Year	Title	Author	Journal / Document type	Risks	Benefits	Why Included (include methods)	Software functions
2009	Clinical decision support capabilities of commercially-available clinical information systems	Wright A, Sittig DF, Ash JS, et al.	*Journal of the American Medical Informatics Association*			The authors conducted a series of interviews with representatives of nine commercially available clinical information systems, evaluating their capabilities against 42 different clinical decision support features. The features can be utilized as a list to evaluate new software.	CDS