U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DEVICES & RADIOLOGICAL HEALTH

REPORT ON RISKS AND BENEFITS TO HEALTH OF NON-DEVICE SOFTWARE FUNCTIONS

November 2020

REPORT ON RISKS AND BENEFITS TO HEALTH OF NON-DEVICE SOFTWARE FUNCTIONS – NOVEMBER 2020

Submitted Pursuant to

Section 3060(b) of the 21st Century Cures Act

U.S. Department of Health and Human Services

Food and Drug Administration

Executive Summary

Section 3060(a) of the 21st Century Cures Act (herein referred to as the Cures Act), enacted on December 13, 2016 (Pub. L. 114-255), amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to exclude certain software functions from the definition of device under section 201(h) of the FD&C Act (21 U.S.C. 321(h)). These software functions are specified in section 520(o)(1) of the FD&C Act and the intended uses of such software functions can be summarized as follows: (1) administrative support of a health care facility; (2) maintaining or encouraging a healthy lifestyle and unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition; (3) serving as electronic patient records when not intended to interpret or analyze patient records; (4) transferring, storing, converting formats, or displaying data; or (5) unless interpreting or analyzing a clinical test or other device data, providing certain types of limited clinical decision support to a healthcare provider.

Section 3060(b) of the Cures Act (herein referred to as section 3060(b)) requires that the Secretary of Health and Human Services (HHS) publish a report every two years that examines information available to the Secretary on any risks and benefits to health associated with the software functions described in section 520(o)(1) of the FD&C Act, and provides summary findings regarding the impact of these non-device software functions on patient safety, including best practices to promote safety, education, and competency. This document is the second report pursuant to section 3060(b) since the enactment of the Cures Act.

In an effort to identify new information published since the Report on Non-Device Software Functions: Impact to Health and Best Practices – December 2018 (herein "the 2018 Report"), the Food and Drug Administration (FDA) collected information from a variety of sources as defined in section 3060(b). This section 3060(b) report includes information reported on or pertaining to United States (U.S.) populations from July 31, 2018 through July 31, 2020 (for all sources).

FDA analyzed the data and information from these sources for evidence regarding impacts to patient safety, benefits and risks to health, and best practices to promote safety, education, and competency associated with the software functions described in section 520(o)(1) of the FD&C Act.

Using the outlined scope and methodology in this report, FDA summarizes its findings from this analysis. In general, the analysis found more benefits than risks to patient safety and health related to these software functions. In addition, this report details best practices related to implementation, training techniques, and use, which could promote safety, education, and competency related to these software functions.

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I. Introduction

Section 3060(a) of the 21st Century Cures Act (herein referred to as the Cures Act), enacted on December 13, 2016 (Pub. L. 114-255), amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to exclude certain software functions from the definition of device under section 201(h) of the FD&C Act (21 U.S.C. 321(h)). These functions are described in section 520(o)(1) of the FD&C Act (21 U.S.C. 360j(o)(1)) and are the focus of this report.

Section 3060(b) of the Cures Act (herein referred to as section 3060(b)) requires a report to be published every two years that examines information available to the Secretary on any risks and benefits to health associated with the software functions described in section 520(o)(1) of the FD&C Act, and provides summary findings on the impact of non-device software functions on patient safety, including best practices. Specifically, section 3060(b) states:

> *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 two years after the date of enactment of this Act and every two years thereafter, that—*
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> *(1) includes input from outside experts, such as representatives of patients, consumers, healthcare 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;*
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> *(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*
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> *(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.*

This document is the 2020 report pursuant to section 3060(b), and includes findings related to information published since the 2018 report.

II. Background

The description of non-device software functions in section 520(o)(1) of the FD&C Act (21 U.S.C. 360j(o)(1)(A)-(E)), as amended by the Cures Act, is the subject of this report. Specifically, section 520(o)(1) of the FD&C Act states:

> *The term device, as defined in section 201(h), shall not include a software function that is intended—*
>
> *(A) for administrative support of a health care facility, including the processing and maintenance of financial records, claims or billing information, appointment*

schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost-effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow;

(B) for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(C) to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as—

(i) such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;

(ii) such records are part of health information technology that is certified under section 3001(c)(5) of the Public Health Service Act; and

(iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(D) for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings; or

(E) unless the function is 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, 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 of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

On September 27, 2019, the Food and Drug Administration (FDA) announced the availability of a section 3060 guidance document to provide FDA's interpretation of section 3060(a) and the types of software that meet and do not meet the device definition in section 201(h), focusing on the first four categories (paragraphs A through D) above. On the same day, FDA announced the

availability of a draft guidance on clinical decision support software, which focuses on the fifth category (paragraph E above). The final and draft guidance documents are referenced below.

1. **Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act:**[1] This guidance explains the effect of the medical software provisions in the Cures Act on preexisting FDA policy, including policy on mobile medical applications; medical device data systems used for the electronic transfer, storage, display, or conversion of medical device data; medical image storage devices used to store or retrieve medical images electronically; medical image communications devices used to transfer medical image data electronically between medical devices; software that automates laboratory workflow; and low-risk general wellness products.
2. **Clinical Decision Support Software:**[2] This draft guidance describes FDA's proposed approach to provide clarity on the scope of FDA's oversight of clinical decision support (CDS) software functions following the changes to the FD&C Act made by section 3060(a) of the Cures Act. When finalized, the guidance will describe FDA's current thinking on types of clinical decision support software functions that: (1) do not meet the definition of a device as amended by the Cures Act; (2) may meet the definition of a device but for which, at this time and based on our current understanding of the risks of these devices, FDA does not intend to enforce compliance with applicable device requirements of the FD&C Act, including, but not limited to, premarket clearance and premarket approval requirements; and (3) meet the definition of a device and on which FDA intends to focus its regulatory oversight.

   This is a draft guidance that, when finalized, will represent the agency's current thinking on these topics; it should not be considered FDA's final approach to or determinations on CDS software as it relates to the Cures Act.

The thinking reflected in these two documents about non-device software functions under section 3060(a) helped to inform the scope of this report.

III. Methodology

Sources. Information used to generate this report came from a variety of sources as defined in section 3060(b). These sources included: consultation with agencies and offices of the Department of Health and Human Services (HHS) involved in health information technology (IT); input from outside experts, such as representatives of patients, consumers, healthcare providers, startup companies, health plans or other third-party payers, venture capital investors, IT vendors, health IT vendors, small businesses, purchasers, employers, and other stakeholders

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-existing-medical-software-policies-resulting-section-3060-21st-century-cures-act
[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-decision-support-software

with relevant expertise; and [other] information available to the [HHS] Secretary on any risks and benefits to health associated with software functions described in section 520(o)(1) [of the FD&C Act]. A list of sources can be found in List of Contributing Sources.

Inclusion/Exclusion Criteria. Parameters for all sources included information reported on or pertaining to United States (U.S.) populations from July 31, 2018 through July 31, 2020. This date range captured new evidence since the publication of the 2018 Report.[3]

Definitions. The Cures Act requires information to be reported about the "impacts to patient safety" and "benefits and risks to health." This report uses the following existing FDA and World Health Organization (WHO) definitions regarding patient safety and health:

- **Impacts to Patient Safety:** A *negative impact* to patient safety is defined as a risk that leads to a serious adverse event (i.e., death, life-threatening, hospitalization, disability or permanent damage, congenital abnormality/birth defect, required intervention to prevent permanent impairment or damage, other serious [important medical events]).[4] By comparison, a *positive impact* to patient safety is defined as reducing the rate of a serious adverse event.
- **Benefits and Risks to Health:** Health is defined as a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.[5]

Analysis Approach. The Cures Act requires a report summarizing findings corresponding to safety, risks and benefits, and best practices categories. Thus, this analysis includes reviews of all sources identified in the Methodology section above to generate the summarized findings of the report. The summaries include information and evidence, regardless of the rigor of the design, the grade of study quality, and strength of evidence, in an effort to provide comprehensive findings.

FDA organized its findings in three categories across the five software functions, which align to the requirements of the Cures Act:

1. Impacts to Patient Safety
2. Benefits and Risks to Health
3. Best Practices to Promote Safety, Education, and Competency

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[3] https://www.fda.gov/media/119187/download
[4] FDA. What is a Serious Adverse Event? https://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm. Accessed August 12, 2020.
[5] World Health Organization. Constitution of WHO: Principles. http://www.who.int/about/mission/en/. Accessed August 12, 2020.

IV. Summary Findings as Required by Section 3060(b) of the 21st Century Cures Act

Many of the 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.[6] We have noted changes in impacts to patient safety and health between the 2018 Report and the current report across each software function. We acknowledge, however, that given there is no requirement to report adverse events from non-device software, adverse events may be underrepresented in this report.

The sections below provide an overview of the findings for each of the five software functions. These software functions are organized into the following three categories to reflect the stated focus of sections 3060(b)(2) and (3): Impacts to Patient Safety, Benefits and Risks to Health, and Best Practices to Promote Safety, Education, and Competency. List of Contributing Sources provides details on all contributing sources cited in the sections below.

A. Administrative Support of a Health Care Facility

Software functions included in this category are defined in section 3060(a) as intended:

> *…for administrative support of a health care facility, including the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost-effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow.*

Impacts to Patient Safety

FDA received three adverse events[7] related to e-prescribing software, which is software that sends a prescription directly from the point of care to the pharmacy.[8] In these events, the software: (1) displayed an incorrect value for an opioid medication order, (2) did not display the correct dosage from a previous medication order, and (3) substituted incorrect medication into a

[6] Submission of adverse event reports involving non-device software is voluntary and not required. As a result, negative impacts to patient safety and health may be underrepresented.

[7] FDA does not substantiate the adverse event reports it receives. Submission of an adverse event report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer, or product caused or contributed to the event. The information in these reports has not been scientifically or otherwise verified as to a cause-and-effect relationship and cannot be used to estimate the incidence of these events. Adverse events included in this report were gathered from MedWatch: The FDA Safety Information and Adverse Event Reporting Program: https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program and Manufacturer and User Facility Device Experience Database - (MAUDE): https://www.fda.gov/medical-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities/manufacturer-and-user-facility-device-experience-database-maude.

[8] Centers for Medicare & Medicaid Services. E-Prescribing. https://www.cms.gov/Medicare/E-Health/Eprescribing/index.html. Accessed July 28, 2020.

patient's drug order without a prompt from the provider. The reports did not cite any impacts on patients' safety resulting from these issues.

FDA received two adverse events[7] related to software functions intended for the management and organization of health practices. One event involved a patient management system incorrectly labeling the attending physician in the providers' patient lists, which the reporter noted could lead to a delay in care if the correct patient is not displayed on the correct provider's patient list. A second event involved clinical orders in an electronic health record (EHR) incorrectly cataloging the order's start date and time as the date and time of order entry. The reporter noted this type of error could lead to a patient receiving treatment earlier than intended.

Changes or additions since last published report: New adverse event types. Information presented in this software function includes adverse events related to management and organization of health practices that were not reported in the 2018 Report.

Benefits and Risks to Health

One retrospective study examined the impact of an automated appointment notification and rescheduling program on no-show appointment rates and appointment wait times. On average, the software reduced the time to see a doctor by 15 days for primary care visits and 24 days for specialty care visits. The study also found that the software reduced appointment no-shows by 1.3% and increased the number of appointments completed by 3.1%.[9]

Changes or additions since last published report: New literature. This report presents information describing the positive impact of an appointment notification and rescheduling program on no-show rates and wait times, a finding not reported in the 2018 Report.

Best Practices to Promote Safety, Education, and Competency

A study reviewed prescription orders from three pediatric clinics using different EHR systems to determine usability issues and associated medication errors. Researchers reviewed 477 orders from Clinic 1, 408 orders from Clinic 2, and 633 orders from Clinic 3; total error rates of prescription orders were 13.2%, 8.8%, and 6.6%, respectively. Researchers evaluated the EHR systems used by these clinics for adherence to the American Academy of Pediatrics (AAP) recommendations for safe and effective e-prescribing. Results indicated that the EHR systems met 21%, 26%, and 47% of the 19 AAP e-prescribing recommendations, respectively. A panel of

[9] Chung, Sukyung, Meghan C. Martinez, Dominick L. Frosch, Veena G. Jones, and Albert S. Chan. "Patient-Centric Scheduling With the Implementation of Health Information Technology to Improve the Patient Experience and Access to Care: Retrospective Case-Control Analysis." *Journal of Medical Internet Research* 22, no. 6 (2020): e16451.

experts found that an EHR system following AAP recommendations could have prevented more than 83% of the study's total prescription errors.[10]

A health IT expert reported that software for administrative support can improve clinician workflow and reduce transcription errors; however, the expert also noted that such software must be accurate and usable for end-users to experience these benefits. To accomplish these objectives, the health IT expert encouraged developers to design software that addresses the needs of end-users and easily integrates into the health practice's existing structure.[11] One study demonstrated the benefits of collecting user feedback to inform software development. In the study, investigators developed a pharmacist-facing dispensary management information system. The researchers' team collected user feedback to make modifications to improve software integration and data sharing. Following system adoption into the practice, users reported high learnability and easy integration into their existing workflow.[12]

A health IT expert noted that users may feel overburdened with alerts from software for administrative support as alerts can cause cognitive overload, leading to user error.[11] Scholars analyzed survey data and interviewed over 2,000 physicians to identify strategies for improving the design of EHR notification inboxes to improve inbox design and efficiency and reduce safety risks associated with information overload from alerts. Findings suggested: "(1) Inbox notification content should be actionable for patient care and relevant to recipient clinician, (2) Inboxes should reduce risk of losing messages, (3) Inbox functionality should be optimized to improve efficiency of processing notifications, (4) Team support should be leveraged to help with EHR inbox notification burden, and (5) Sufficient time should be provided to all clinicians to process EHR inbox notifications."[13]

Changes or additions since last published report: All information is new since the publication of the 2018 Report.

B. Maintaining or Encouraging a Healthy Lifestyle

Software functions included in this category are defined in section 3060(a) as intended:

> *…for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.*

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[10] Gildon, Brooke L., Michelle Condren, and Christine C. Hughes. "Impact of electronic health record systems on prescribing errors in pediatric clinics." *Healthcare*, vol. 7, no. 2, p. 57. Multidisciplinary Digital Publishing Institute, 2019.
[11] Expert Interviews for the Fulfillment of the 21st Century Cures Act Section 3060 Required Report in the Appendix. July 2020.
[12] Fisher, Arielle M., Timothy M. Mtonga, Jeremy U. Espino, Lauren J. Jonkman, Sharon E. Connor, Nickie K. Cappella, and Gerald P. Douglas. "User-centered design and usability testing of RxMAGIC: a prescription management and general inventory control system for free clinic dispensaries." *BMC Health Services Research* 18, no. 1 (2018): 703.
[13] Murphy, Daniel R., Tyler Satterly, Traber D. Giardina, Dean F. Sittig, and Hardeep Singh. "Practicing clinicians' recommendations to reduce burden from the electronic health record inbox: a mixed-methods study." *Journal of General Internal Medicine* 34, no. 9 (2019): 1825-1832.

Impacts to Patient Safety

Changes or additions since last published report: No changes. The analysis of all sources identified no new direct impacts to patient safety. This finding is consistent with the 2018 Report, which also reported no direct impacts to patient safety.

Benefits and Risks to Health

Two studies evaluated the impact of mobile health software on health-promoting behaviors. The first—a pilot study—examined the impact of a mobile-phone automated texting intervention on blood pressure (BP) self-monitoring and patient self-management in adults with hypertension. The intervention was designed to prompt participants to take their BP by sending text message reminders at self-selected times. Results showed high adherence to BP self-monitoring (79%) during the intervention period. Patients noted that the intervention increased their perceived importance of BP self-monitoring, medication adherence, healthy diet and exercise, and stress management.[14] Evidence from a second study suggested that mobile health applications are associated with increased engagement with health-promoting behaviors among adults with chronic conditions. These behaviors included tracking health-related goals, making health-related decisions, and engaging in health-related discussions with care providers.[15]

Three studies examined the effect of mobile phone applications and wearable technology on diet, weight loss, and quality of life. The first study tested the effectiveness of a smartphone application developed to predict dietary lapses. Participants using the application experienced a reduction in unplanned dietary lapses, and a decrease in body weight and body mass index.[16] A second study—a randomized control trial—tested the effectiveness of an application developed to increase food pantry clients' incorporation of vegetables into their diets. The application offered users vegetable-based recipes and healthy cooking tips. Results of the trial suggested that the use of the mobile application encouraged cooks to prepare healthier meals by increasing the use and assortment of vegetables in meal preparations.[17] Last, a prospective cohort study of adolescent and young adult patients with cancer examined the impact of digital wearable

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[14] Irizarry, Taya, Matthew Allen, Brian P. Suffoletto, Julian Einhorn, Lora E. Burke, Thomas W. Kamarck, Bruce L. Rollman, and Matthew F. Muldoon. "Development and Preliminary Feasibility of an Automated Hypertension Self-Management System." *The American Journal of Medicine* 131, no. 9 (2018): 1125-e1.

[15] Mahmood, Asos, Satish Kedia, David K. Wyant, SangNam Ahn, and Soumitra S. Bhuyan. "Use of mobile health applications for health-promoting behavior among individuals with chronic medical conditions." *Digital Health* 5 (2019): 2055207619882181.

[16] Forman, Evan M., Stephanie P. Goldstein, Fengqing Zhang, Brittney C. Evans, Stephanie M. Manasse, Meghan L. Butryn, Adrienne S. Juarascio, Pramod Abichandani, Gerald J. Martin, and Gary D. Foster. "OnTrack: development and feasibility of a smartphone app designed to predict and prevent dietary lapses." *Translational Behavioral Medicine* 9, no. 2 (2019): 236-245.

[17] Clarke, Peter, Susan H. Evans, and Deborah Neffa-Creech. "Mobile app increases vegetable-based preparations by low-income household cooks: a randomized controlled trial." *Public Health Nutrition* 22, no. 4 (2019): 714-725.

technology on health-related quality of life (HRQOL). Results demonstrated that the use of digital wearable technology to track physical activity was associated with significant improvements in eight dimensions of HRQOL (i.e., physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, energy/fatigue, pain, and general health perceptions).[18]

Changes or additions since last published report: No changes. The analysis of all sources, including two studies evaluating the impact of mobile health software on health-promoting behaviors and three studies examining the impact of mobile phone applications and wearable technology on diet, weight loss, and quality of life, identified no new direct benefits or risks to health. New information presented for this software function is consistent with information presented in the 2018 Report.

Best Practices to Promote Safety, Education, and Competency

A health IT expert noted that while many applications use software functions in the category of maintaining or encouraging a healthy lifestyle, the applications often lack evidence to support claims that the software function is beneficial to health. To filter out applications that are ineffective at maintaining or encouraging a healthy lifestyle, the expert suggested that these software functions undergo preliminary testing to evaluate their impact on user behavior and ensure they are evidence based.[11] In terms of software function effectiveness, the expert also suggested developers tailor the software to end-users' conditions and include a feedback loop of data between users and their clinicians so the clinicians can provide individual recommendations to users.[11]

Changes or additions since last published report: All information is new since the publication of the 2018 Report.

C. Electronic Patient Records

Software functions included in this category are defined in section 3060(a) as intended:

> *…to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as—*
>
> *(i) such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;*
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> *(ii) such records are part of health information technology that is certified under section 3001(c)(5) of the Public Health Service Act; and*

[18] Yurkiewicz, Ilana R., Pamela Simon, Michaela Liedtke, Gary Dahl, and Tamara Dunn. "Effect of Fitbit and iPad wearable technology in health-related quality of life in adolescent and young adult cancer patients." *Journal of Adolescent and Young Adult Oncology* 7, no. 5 (2018): 579-583; Hays, Ron D., and Leo S. Morales. "The RAND-36 measure of health-related quality of life." *Annals of Medicine* 33, no. 5 (2001): 350-357. https://www.rand.org/pubs/reprints/RP971.html.

(iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.

Impacts to Patient Safety

One study analyzed patient safety reports from three large academic healthcare institutions and found a negative association between EHR usability and medication error rates. Of the 9,000 patient safety reports reviewed, 5,079 were related to both the EHR system and medication. Of these 5,079 reports, 3,243 (36%) cited EHR usability as a contributing factor to patient safety events. Of these 3,243 reports, 609 (18.8%) instances of safety events reached the patient: 201 did not cause harm, 109 required an intervention to prevent harm, 20 led to temporary harm, and the consequences were unknown in 279 cases. Over half of the 609 errors that reached the patient were improper doses associated with either the EHR not providing appropriate feedback to the user or usability issues from a confusing or cluttered EHR information visual display.[19]

FDA received one adverse event report[7] related to this software function. The report was related to textual notes displaying the previous patient's information, instead of the current patient. The report did not cite any impact on the patient's safety resulting from this issue.

Changes or additions since last published report: New literature. This report presents information describing the impact of EHR medication errors on patient safety, a finding not reported in the 2018 Report.

Benefits and Risks to Health

A study examined the relationship between EHR adoption and hospital mortality rates. Researchers measured three components of EHR adoption: the baseline level of EHR adoption, the maturation of the baseline functions over time, and the adoption of new EHR functions. Findings suggest that while baseline adoption of EHRs was associated with an increase in mortality rates, maturation and adoption of new EHR functions were associated with reduced mortality rates. Average EHR adopters experienced lower hospital mortality rates than nonadopters. Researchers noted that small and nonteaching hospitals may initially experience higher mortality rates upon adopting an EHR because they have fewer resources to support EHR implementation relative to large teaching hospitals. However, across all hospitals, findings suggested that as EHR systems mature, hospital mortality rates decline.[20]

A retrospective study assessed the association between the meaningful use of EHR systems, quality of care, and outcomes of patients with schizophrenia. Findings suggest providers who used EHR systems across four of the Healthcare Effectiveness Data and Information Set

[19] Ratwani, Raj M., Erica Savage, Amy Will, Allan Fong, Dean Karavite, Naveen Muthu, A. Joy Rivera, et al. "Identifying electronic health record usability and safety challenges in pediatric settings." *Health Affairs* 37, no. 11 (2018): 1752-1759.
[20] Lin, Sunny C., Ashish K. Jha, and Julia Adler-Milstein. "Electronic health records associated with lower hospital mortality after systems have time to mature." *Health Affairs* 37, no. 7 (2018): 1128-1135.

(HEDIS®) quality of care measures specific to mental health (i.e., diabetes screening, diabetes monitoring, cardiovascular monitoring, and antipsychotic medication adherence) delivered a higher quality of care to patients with schizophrenia than providers who did not use EHR systems. Patient outcomes for providers who used EHR systems (relative to non-EHR providers) were significantly better, "as measured by fewer patients with psychiatric inpatient admission and emergency department (ED) visits, as well as fewer patients with elevated laboratory values for diabetes and cardiovascular disease."[21]

A retrospective observational study analyzed outcomes associated with integrating patient-generated health data (PGHD) and EHR systems at a multispecialty practice. Pregnant patients uploading PGHD to the EHR patient portal experienced a significant drop in average post-partum body mass index (BMI) relative to pregnant patients who did not upload PGHD to the patient portal. Among patients with chronic disease, findings demonstrated that self-monitored blood glucose PGHD uploaded to the patient portal was associated with a reduction in hemoglobin A1c (HbA1c) and BMI. The researchers noted that it is unclear whether changes in HbA1c and BMI were due to PGHD upload, patient motivation, or changes in medical management.[22] A second retrospective study examined the association between access to a patient portal and improved outcomes for patients with diabetes. Findings suggest that providing patients with computer and mobile patient portal access "significantly improved adherence to diabetes medication and glycemic control, with greater benefits among patients with more clinical need."[23]

A 12-month randomized study tested whether a mobile personal health record (mPHR) app could improve the quality of medical care (i.e., receipt of cardiometabolic and preventative services) for individuals treated in a behavioral health home. Participants randomized into the intervention arm used a mPHR app to view information on diagnoses, laboratory results, medications, and health goals. At the end of the 12-month study, participants randomized into the intervention arm maintained a high quality of care while participants in the control arm experienced a statistically significant, though modest, decline in quality of care.[24] A second study identified an association between patient portal use and health care utilization. The findings of this observational study

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[21] Ng-Mak, Daisy, and Charles Ruetsch. "Association between meaningful use of electronic health records and patient health outcomes in schizophrenia: a retrospective database analysis." *The American Journal of Managed Care* 25, no. 9 Suppl (2019): S159-S165.
[22] Ancker, Jessica S., Elizabeth Mauer, Robin B. Kalish, Joshua R. Vest, and J. Travis Gossey. "Early adopters of patient-generated health data upload in an electronic patient portal." *Applied Clinical Informatics* 10, no. 02 (2019): 254-260.
[23] Graetz, Ilana, Jie Huang, Emilie R. Muelly, Bruce Fireman, John Hsu, and Mary E. Reed. "Association of mobile patient portal access with diabetes medication adherence and glycemic levels among adults with diabetes." *JAMA Network* 3, no. 2 (2020): e1921429-e1921429.
[24] Druss, Benjamin G., Jianheng Li, Stephanie Tapscott, and Cathy A. Lally. "Randomized Trial of a Mobile Personal Health Record for Behavioral Health Homes." *Psychiatric Services* (2020): appi-ps.

suggest access to a patient portal was significantly associated with patients' visit rates. Patients with diabetes and patients with multiple complex conditions had a significantly higher rate of outpatient visits. Among patients with multiple complex chronic conditions, patient portal use was significantly associated with fewer ED visits and preventable hospital stays.[25]

Changes or additions since last published report: New literature. This report presents information describing the positive impact of EHR adoption on mortality rates and the effect of EHRs and mPHR applications on quality of care and patient outcomes, findings not reported in the 2018 Report.

Best Practices to Promote Safety, Education, and Competency

A study analyzed the frequency of errors in ambulatory visit notes in patient portals. Almost 30,000 patients from three different health systems responded to a survey that included questions on instances and severity of mistakes in visit notes. Of the patients surveyed, 4,830 reported a perceived mistake, of whom 1,563 considered the mistake to be "somewhat serious" and 480 considered the mistake to be "very serious."[26] To address errors in EHR data, a health IT expert recommended that EHR system vendors implement monitoring protocols to ensure data are entered correctly. The expert also suggested vendors provide patients with the ability to review and request edits to their electronic medical records (EMRs) in the instance that information is incorrect. To streamline this process, the health IT expert proposed encouraging health systems to employ dedicated staff to monitor EHR system data for correctness and attend to patients who request revisions to incorrect data.[11] A public commenter noted that their organization employs a team of clinicians to monitor and review data from patient visits and medication orders to ensure that the organization aligns its standards of care with safety policies. The public commenter said that if the clinician team finds errors in the data or software, the team identifies the root causes and develops a risk mitigation strategy to fix the error.[27]

In terms of usability and safety, scholars have advocated for vendors to be more transparent regarding issues identified in their EHR systems to avoid potential adverse events. Researchers have encouraged hospitals and health systems to utilize EHR safety assessment test case scenarios and suggested the federal government mandate EHR usability and safety testing and reporting to identify and remedy potential errors in EHR systems.[28] Health care technology experts agree with scholars' sentiments and suggest EHR system vendors communicate with

[25] Reed, Mary E., Jie Huang, Richard J. Brand, Romain Neugebauer, Ilana Graetz, John Hsu, Dustin W. Ballard, and Richard Grant. "Patients with complex chronic conditions: health care use and clinical events associated with access to a patient portal." *PLOS One* 14, no. 6 (2019): e0217636.
[26] Bell, Sigall K., Tom Delbanco, Joann G. Elmore, Patricia S. Fitzgerald, Alan Fossa, Kendall Harcourt, Suzanne G. Leveille, et al. "Frequency and Types of Patient-Reported Errors in Electronic Health Record Ambulatory Care Notes." *JAMA Network* 3, no. 6 (2020): e205867-e205867.
[27] Response to the Development of 21st Century Cures Act Section 3060 Required Report Request for Input. July 2020.
[28] Ratwani, Raj M., Michael Hodgkins, and David W. Bates. "Improving electronic health record usability and safety requires transparency." *JAMA Network*, no. 24 (2018): 2533-2534.

end-users across the product lifecycle to better integrate their EHR systems with the daily activities of end-users and other software that might interact with the EHR systems.[11] A public commenter noted that their software development process involves collaboration between developers and users. Following software development, the public commenter said their developers guide end-user organizations through the implementation and adoption process and assist in setting up a program to keep track of impacts to clinical workflow. When issues arise, the public commenter's surveillance program tracks potential risks to patient safety and deploys the necessary resources to resolve the problem.[27]

Regarding standards for data transfer, a public commenter noted the need for data standardization in EHR systems to ensure accurate transfer of data between unregulated software products and regulated medical devices. The commenter mentioned possible benefits of interoperability while highlighting potential risks and considerations that are important to maintain data integrity of these functions.[27]

In terms of end-user education and competency, health care technology experts suggested vendors offer short education vignettes, instead of traditional learning sessions and instructional manuals. Short vignettes, the experts noted, can be consumed in five minutes or less, capture the attention of the user, and provide valuable information.[11]

Changes or additions since last published report: All information is new since the publication of the 2018 Report.

D. Transferring, Storing, Converting Formats, or Displaying Clinical Laboratory Test or Other Device Data and Results

Software functions included in this category are defined in section 3060(a) as intended:

> *…for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings.*

Impacts to Patient Safety

Changes or additions since last published report: No changes. The analysis of all sources identified no new direct impacts to patient safety. This finding is consistent with the 2018 Report, which also reported no direct impacts to patient safety.

Benefits and Risks to Health

A pilot feasibility study assessed health care professional's (HCP) use of an integrative software platform designed to collect and display diabetes data from multiple devices. Results showed a significant increase in the number of times HCPs referred to the data in interactions with patients (i.e., from 2.8 to 6.1 times per visit) and an increase in patient engagement with data (i.e., from

61% to 94%). Findings suggested an integrative software platform can increase patient and provider interaction with data without adversely affecting visit length or clinic workflow.[29]

Changes or additions since last published report: New literature. The information presented in this report offers evidence supporting benefits to health of software functions intended for transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results. The 2018 Report did not identify any benefits or risks to health relative to this software function.

Best Practices to Promote Safety, Education, and Competency

Medical informatics experts reported that testing software intended for transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results requires the collection of many data points and application of complex math equations that can be difficult to evaluate for accuracy. While the medical informatics experts noted major hospitals may be able to conduct periodic software testing, they stressed the need for developers to take ownership of addressing potential transmission errors by frequently monitoring and updating their products to ensure proper functionality.[11] A health IT expert also highlighted difficulties in maintaining the integrity of data transferred between different platforms and suggested developers conduct continuous software testing to address degradation issues that can distort images during compression and transfer.[11]

To address challenges with transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results, a medical diagnostic expert noted their company develops software in accordance with FDA device regulations, even if their products are not defined as devices. The medical diagnostic expert also recommended adoption of nationally recognized standards for maintaining information security.[11] Health care technology experts further expressed the importance of these software functions using internationally recognized standards, such as the Digital Imaging and Communications in Medicine (DICOM) standards, for transmitting, storing, retrieving, printing, processing, and displaying medical imaging information.[30]

Changes or additions since last published report: All information is new since the publication of the 2018 Report.

E. Limited Clinical Decision Support

Software functions included in this category are defined in section 3060(a) as intended:

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[29] Wong, Jenise C., Zara Izadi, Shannon Schroeder, Marie Nader, Jennifer Min, Aaron B. Neinstein, and Saleh Adi. "A pilot study of use of a software platform for the collection, integration, and visualization of diabetes device data by health care providers in a multidisciplinary pediatric setting." *Diabetes Technology & Therapeutics* 20, no. 12 (2018): 806-816.

[30] Digital Imaging and Communications in Medicine. https://www.dicomstandard.org/. Accessed July 28, 2020.

…unless the function is 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, 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 of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

Impacts to Patient Safety

A case study measured the safety performance of operational clinical decision support (CDS) software within EHR systems to analyze how effectively the software alerted clinicians to potential adverse drug events. The exposure involved simulated medication orders to determine if the EHR systems correctly generated an alert, warning, or soft or hard stop when a clinician entered a test order that was likely to cause patient harm. The researchers noted that while the mean overall test score (53.9% in 2009 and 65.5% in 2018), and hospital scores for basic (69.8% in 2009 and 85.6% in 2018) and advanced (29.6% in 2009 and 46.1% in 2018) CDS increased between 2009 and 2018, there was wide variation in safety performance, which suggests safety vulnerabilities persist in CDS software within EHR systems.[31]

A second study examined the incidence of adverse drug events following providers overriding medication-related CDS alerts. Reviewers determined that 81.6% (1,998 appropriate overrides out of 2,448 total overrides) of the providers' overrides were appropriate. Clinicians administered medication after overriding 1,636 alerts from the CDS software. Following clinicians overriding alerts and administering medication, there were more than 50 potential adverse drug events and four definite adverse drug events. Findings showed that inappropriate overrides of the CDS software by clinicians were associated with a 600% increase in the risk of an adverse drug event and length of intensive care unit stay.[32]

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[31] Classen, David C., A. Jay Holmgren, Lisa P. Newmark, Diane Seger, Melissa Danforth, and David W. Bates. "National trends in the safety performance of electronic health record systems from 2009 to 2018." *JAMA Network* 3, no. 5 (2020): e205547-e205547.

[32] Wong, Adrian, Mary G. Amato, Diane L. Seger, Christine Rehr, Adam Wright, Sarah P. Slight, Patrick E. Beeler, E. John Orav, and David W. Bates. "Prospective evaluation of medication-related clinical decision support over-rides in the intensive care unit." *BMJ Quality & Safety* 27, no. 9 (2018): 718-724.

A third study—a systematic literature review—presented evidence suggesting that use of CDS software tools increases the number of prescriptions for correct medications or dosages and improves the receipt of recommended laboratory monitoring and appropriate treatment in response to abnormal test results.[33]

FDA received four adverse event reports[7] 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.

Changes or additions since last published report: New literature and adverse event types. This report identified new evidence describing variation in safety performance relative to medication events across software functions intended for limited clinical decision support, a finding not reported in the 2018 Report.

Benefits and Risks to Health

One prospective cohort study assessed the impact of an electronic medical record (EMR)-linked CDS software intended for healthcare providers on opioid prescription amounts, patient completion of opioid abuse risk mitigation strategies, rate of hospitalizations, and ED use. The CDS software prompts providers to have their patients complete overdue risk mitigation tasks (i.e., urine drug screening, naloxone prescriptions, referrals to specialty care) and prompts providers to complete the Opioid Risk Tool to assess their patient's risk of opioid abuse. While changes in high-dose opioid prescription amounts and rate of hospitalizations were insignificant, results did show a significant increase in the completion of risk mitigation strategies and a decrease in ED use after implementation of the CDS software.[34] Another study examined the effectiveness of best practice CDS alerts on the rate of lumbar imaging in ambulatory care settings. Upon implementation of the CDS alert, findings showed a statistically significant

[33] Whitehead, Nedra S., Laurina Williams, Sreelatha Meleth, Sara Kennedy, Nneka Ubaka-Blackmoore, Michael Kanter, Kevin J. O'Leary, et al. "The Effect of Laboratory Test–Based Clinical Decision Support Tools on Medication Errors and Adverse Drug Events: A Laboratory Medicine Best Practices Systematic Review." *The Journal of Applied Laboratory Medicine* 3, no. 6 (2019): 1035-1048.

[34] Price-Haywood, Eboni G., Jeffrey Burton, Todd Burstain, Jewel Harden-Barrios, John Lefante, Lizheng Shi, Robert N. Jamison, Alessandra Bazzano, and Lydia Bazzano. "Clinical Effectiveness of Decision Support for Prescribing Opioids for Chronic Noncancer Pain: A Prospective Cohort Study." *Value in Health* 23, no. 2 (2020): 157-163.

decrease in the overall rate of imaging (9.6%) and magnetic resonance imaging (14.9%).[35] A third study assessed the impact of CDS software tools on cardiovascular (CV) risk. Results showed clinics using CDS experienced a statistically significant reduction in 10-year CV risk trajectory compared to clinics without CDS. Researchers also found that primary care providers in clinics using CDS engaged in more frequent discussions of CV risk reduction and felt better prepared to discuss priorities with patients.[36]

Changes or additions since last published report: New literature. This report presents information describing the positive impact of CDS software on opioid care management, lumbar imaging rates, and CV risk, findings not reported in the 2018 Report.

Best Practices to Promote Safety, Education, and Competency

Medical informatics experts expressed concern that providers may rely too heavily on CDS software to determine appropriate treatments.[11] Given this point, scholars emphasized that CDS software is most effective when used to support the expert opinion of providers. These scholars noted that combining provider insight with CDS support can limit the risk of inaccurate diagnostic or treatment recommendations.[37]

The medical informatics experts also noted that software users are often unaware of the complex series of steps CDS software goes through to offer a recommendation. Experts said this lack of understanding can limit the usability of the software and make it difficult for clinicians to locate where an error occurred when the CDS software recommends an inappropriate treatment. To inform users on these processes, a medical diagnostics expert recommended using demos and onscreen guidance to educate clinicians on the effective use of CDS software.[11]

Scholars analyzed results from a safety performance assessment that used simulated medication orders to evaluate how many medication-related errors CDS software within an EHR system prevented between 2009 and 2016. The study found that the average CDS software prevented 54% of potential adverse drug events in 2009 and 61.6% of such errors in 2016. Results showed hospitals that took the safety performance assessment test more than once experienced better outcomes than hospitals undergoing the assessment for the first time.[38] A public commenter noted that the safe use of CDS software depends on organizations following safe practices. The

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[35] Chen, Doris, Hriday P. Bhambhvani, Jason Hom, Megan Mahoney, Max Wintermark, Christopher Sharp, John Ratliff, and Yi-Ren Chen. "Effect of Electronic Clinical Decision Support on Imaging for the Evaluation of Acute Low Back Pain in the Ambulatory Care Setting." *World Neurosurgery* 134 (2020): e874-e877.
[36] Sperl-Hillen, JoAnn M., A. Lauren Crain, Karen L. Margolis, Heidi L. Ekstrom, Deepika Appana, Gerald Amundson, Rashmi Sharma, Jay R. Desai, and Patrick J. O'Connor. "Clinical decision support directed to primary care patients and providers reduces cardiovascular risk: a randomized trial." *Journal of the American Medical Informatics Association* 25, no. 9 (2018): 1137-1146.
[37] Anderson, Michael, and Susan Leigh Anderson. "How should AI be developed, validated, and implemented in patient care?" *AMA Journal of Ethics* 21, no. 2 (2019): 125-130.
[38] Holmgren, A. Jay, Lisa Newmark, Melissa Danforth, David Classen, and David Bates. "Assessing the safety of electronic health records: a national longitudinal study of medication-related decision support." *BMJ Quality & Safety* 29, no. 1 (2020): 52-59.

commenter said that organizations are responsible for: 1) deciding how the software is configured in their practice, 2) providing sufficient training to their staff, and 3) collecting comprehensive and accurate data from patients. To ensure patient safety, the commenter said organizations must select a suitable software configuration and adoption process.[27]

Medical informatics experts expressed that CDS software needs to undergo rigorous testing to ensure it returns accurate results before developers deploy the software to end-users. Experts suggested making developers and vendors the primary focus of safety and usability training for this software.[11] A public commenter noted developers can mitigate risks posed by CDS software by establishing a rigorous editorial process for their content. The commenter suggested developers: 1) employ multidisciplinary teams of clinical experts to create content, 2) use formal grading methodology, and 3) have outside reviewers assess their products for accuracy. The commenter also noted that developers should review and update content regularly. In instances where developers are not creating their own content, they should ensure that their source follows similar rigorous editorial procedures.[27]

In terms of best practices for implementing drug-drug interaction (DDI) alerts, a public commenter suggested organizations create a committee responsible for determining CDS software DDI alert filters and restrictiveness. The commenter also suggested conducting annual reviews of alert filters, alert log data, and adverse events to identify changes that need to be made to filter settings.[27]

Changes or additions since last published report: All information is new since the publication of the 2018 Report.

V. Appendix: List of Contributing Sources

FDA compiled the following list of contributing sources by the information collection activities it conducted to generate the findings summarized in this report.

Expert Interviews

- Philips – July 10, 2020
- Roche – July 10, 2020
- Office of the National Coordinator for Health Information Technology (ONC) – July 15, 2020
- American Medical Informatics Association (AMIA) – July 16, 2020

Public Comments

- FY20 Development of 21st Century Cures Act Section 3060 Required Report Request for Input: https://www.regulations.gov/document?D=FDA-2018-N-1910-0024

Peer-Reviewed Literature

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- FDA Guidance, Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-existing-medical-software-policies-resulting-section-3060-21st-century-cures-act.
- FDA Guidance Documents: https://www.fda.gov/regulatoryinformation/guidances/.

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- Medical Device Reporting (MDR) database: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMDR/Search.cfm.
- MedWatch: The FDA Safety Information and Adverse Event Reporting Program: https://www.fda.gov/safety/medwatch/.
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- World Health Organization: http://www.who.int/about/mission/en/.