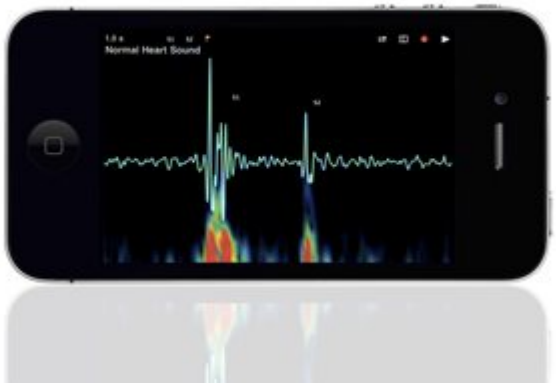
Regulatory Challenges in Mobile Medical Applications

Posted 25 September 2018 | By Loganathan Kumarasamy, MS, Stephen F. Amato, PhD, MBA, RAC

This article presents the challenges associated with the regulation of mobile medical applications compared to computer software. The authors identify the differences between mobile applications and computer systems to determine the practical challenges of regulating these mobile applications as Software as a Medical Device (SaMD). This article also highlights various principles that can be followed to ensure patient safety and wellness by mobile application manufacturers.



Introduction

The consciousness of the growing population toward health has promoted the rapid growth of mobile applications (apps), making it a key component in the future of digital health. Regulations need to evolve continuously to correspond to such technical advancements in this dynamic digital era. In December

2017, FDA issued a guidance in which mobile applications would be regulated as Software as a Medical Device (SaMD). However, operational differences between computer software and mobile software make FDA's approach arguable.

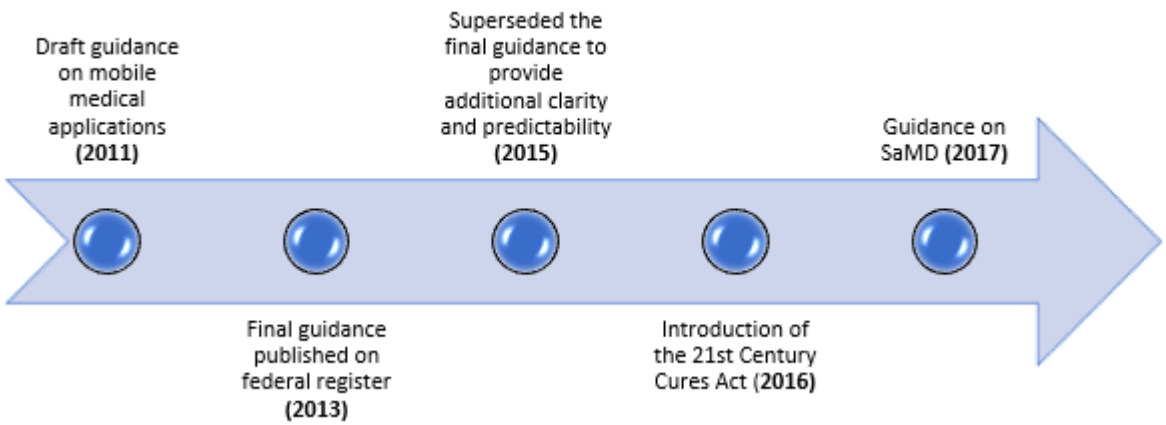
The instant connectivity and flexibility provided by mobile applications are transforming the world by transporting us into a new era of advancement and making information readily accessible. The digitalization of healthcare systems has provided physicians and medical technicians with opportunities to improve diagnostic techniques and treatment plans for the well-being of patients. Patients also benefit from easy appointment scheduling, instant access to treatment plans, medication reminders and trackers for fitness and dietary plans. Though these applications offer several advantages, it is important to understand the underlying risks to patient safety and Patient Health Information (PHI).

As of 2017, there are approximately 259,000 mobile medical applications of which approximately 100 are regulated as medical devices. About 65% of these applications are general wellness apps and the rest focus on nutrition, patient treatment and chronic disease management.[1] These numbers continue to grow tremendously and are expected to reach 635,000. This rapid growth poses a question about the regulation, data security and control of these mobile medical applications. The following discussion will examine the regulatory focus on these applications, challenges and recommended steps to address these challenges.

FDA's Path to Mobile Medical Applications

Considering the rapid growth of mobile applications and mobile medical devices, there was a strong need to regulate these applications to ensure patient safety. Several mobile applications were used as stand-alone medical devices or in conjunction with hardware components. **Figure 1** explains the path of FDA's oversight of mobile medical applications.

Figure 1. FDA's Mobile Medical Applications Guidance.



In July 2011, FDA issued a draft guidance about its intent to regulate mobile medical applications, which was primarily focused on applications meeting the definition of "device." FDA clarified that applications that do not meet the definition of "device" will not be regulated or enforced under regulatory requirements.[2] In September 2013, FDA published guidance on mobile medical applications in the Federal Register.

Further, in February 2015, FDA issued guidance on mobile medical applications, *Mobile Medical Applications: Guidance for Industry and FDA Staff,* explaining the current perspective and FDA's consideration in regulating mobile medical applications, which superseded the 2013 issued guidance.[3]

Risk-Based Approach

With the introduction of the *21st Century Cures Act* (December 2016), the definition of medical device was altered to exclude certain software functions that possessed low risk to patient safety.[4] On 8 December 2017, FDA issued guidance, *Software as a Medical Device (SaMD): Clinical Evaluation,* adopting the guidance from International Medical Device Regulators Forum (IMDRF).[5] With this guidance, the previous guidance was amended with a disclaimer that FDA would revise the guidance as part of a digital action plan. As per the latest guidance, mobile medical applications are considered Software as a Medical Device (SaMD). The guidance mandates the analytical and clinical validation of the application. A risk-based approach was established as part of this guidance, highlighting the need to regulate high-risk applications, excluding the less important or low-risk items. FDA also has highlighted the same as part of their *Digital Health Innovation Action Plan*, where it was mentioned FDA will enforce compliance only on mobile applications with "high" risk, excluding the low risk ones.[6] From a manufacturers' perspective, it is important the risk associated with the application being developed is

assessed as part of design and the application is appropriately classified. The risk-based approach indicates the mobile applications with high risk to the safety of patient, will be considered as Software as a Medical Device (SaMD) and regulated accordingly.

The latest risk-based classification of SaMD is the electrocardiogram (ECG) app that will be introduced into the market by Apple on their watches. FDA has classified this application as Class II medical device with restrictions on labeling and usage of the application. It is interesting to see that the labeling should include the note that the device is not for diagnosis purposes and to be used only for information purposes; however, the device will be regulated as Class II medical device for over-the-counter use. These advancements provide a perfect example of how FDA has moved its focus based on risk-based approach.

Can mobile applications be considered as software similar to computer systems?

Based on the definition of SaMD, mobile applications are considered as software and are regulated in a similar manner.

However, this uncovers several gaps and poses questions due to the inherent differences between mobile applications and computer software.

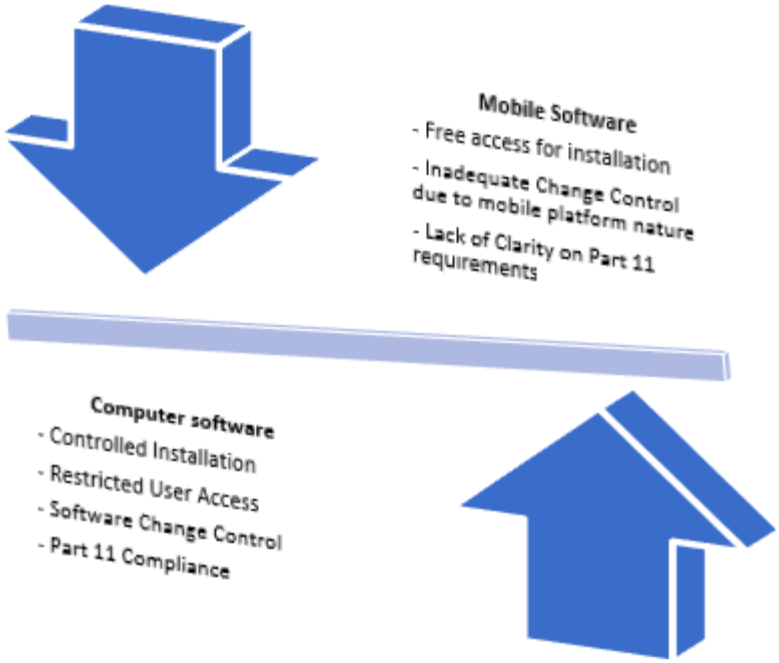
The following are some of the practical differences which present regulatory challenges for mobile medical applications:

- How effectively can change control be implemented for mobile applications? Unlike the Operating Systems (OS) of computers, the OS of mobile applications are not controlled completely by the users, leading to a gap in the change control process of software, thereby questioning usability and data collection.
- With increased threat from cybersecurity attacks, there is a strong need for additional regulatory requirements for mobile applications to ensure comprehensive patient data protection in comparison to computer applications.
- Regulatory and compliance checks on computer software can be performed during software installation (e.g., security, user access) and deployment, whereas mobile applications have a free platform and can be downloaded and accessed by anyone. This makes it challenging to ensure the applications are used only by the intended users.
- In addition to mobile applications being considered as medical devices, there are several mobile

applications that could be utilized in clinical trial processes, replacing or supplementing electronic Patient Record Outcomes (ePROs), Electronic Data Capture (EDC) tools, etc. This prompts additional regulatory requirements for protecting clinical data and ensuring data integrity in the GCP space.

- Will the records within the mobile applications be considered as electronic records and consequently invoke the application of Part 11 requirements?

Figure 2. Key Differences Between Mobile Software and Computer Software



How can these challenges be addressed?

While FDA and other regulatory agencies come up with concrete sets of requirements for mobile applications, it is important that manufacturers and sponsors, who are utilizing the mobile applications, perform their due diligence to ensure patient safety and data protection. To address the key regulatory requirements, classify the mobile medical application into one of the following categories and follow the recommended steps provided in the table below:

- medical device
- wellness app

- clinical support
- other medical category

Table 1. Healthcare Mobile Applications and Recommended Steps for Compliance.

Category	Recommended Steps
Medical Devices	• Follow the requirements as outlined by FDA under the SaMD category if it meets the definition of medical device • Identify the risk category and ensure appropriate controls are placed • Ensure developers utilized for the development are properly trained on software principles and adequate testing is performed at each stage • Ensure adequate data security controls exist within the application and cybersecurity testing is performed • Define the intended use of the application clearly with adequate guidelines on dos and don'ts • Ensure appropriate procedures are in place to test the application in case of change in the OS and release patches, if required, to meet the OS updates • Ensure the mobile medical application is clinically and analytically validated prior to FDA filings
Wellness Apps	• FDA intends to exercise enforcement discretion on wellness applications which pose low risk to patients. FDA does not expect the sponsor to submit premarket applications. • It is critical the manufacturers do not claim any capability around diagnosis, treatment or prevention of diseases with the use of such applications.

Clinical Support Applications and Other Critical Medical Category Applications	• Define and identify the risks to determine if the application belongs to high or low-risk category • For high-risk category, ensure adequate software development and change control processes are implemented. • Provide guidelines or help texts with the application to ensure it is utilized as per intended usage • Identify ways to restrict the usage of the application by providing access control • Sponsors who are utilizing mobile applications for clinical trials should ensure the application is validated and data protection controls are available. • Sponsors also should ensure patients are comfortable using the mobile applications and alternate mechanisms should be put in place to address gaps.

Conclusion

With technical advancements come risks and oversight. Sponsors and manufacturers should ensure they follow the appropriate guidance and additional steps to ensure patient safety without compromising on data protection. It is important to understand that SaMD is not the only critical area, but there are also several other mobile applications utilized for various purposes that could have an impact on patient safety. FDA and other regulatory agencies should come forward to address these gaps and define a clear path for all medical applications beyond the SaMD category. It is also important that a periodic review is performed on a frequent basis to meet regulatory challenges due to rapid technical improvements.

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Loganathan Kumarasamy, MS, is responsible for managing validation and compliance services at Zifo RnD Solutions. He holds a Master's degree in regulatory affairs from Northeastern University and has been working as a senior consultant for more than seven years. With in-depth knowledge of Part 11, EU Annex 11, HIPAA, data integrity principles and applicable GxP regulations for computer systems, medical devices and laboratory systems, he has been providing consultation for top pharmaceutical and product development companies. He can be reached at Loganathan.k@zifornd.com

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