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Mobile Medical Applications (MMAs)

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Introduction

Mobile communication devices, particularly smartphones, are radically changing the way we think and make decisions about our health care. Over the last decade, smartphones and applications have changed several important aspects of our lives, not just our entertainment options but also how we track personal finances, shop, travel and interact with friends and family.

Health care technologies, such as mobile health tracking applications (mHealth apps) and activity monitors, have crept into our lives, and many of us routinely and actively engage with them. In fact, Jawbone, a manufacturer of popular wearable fitness trackers, proclaimed in a recent article that users spend more time with their Jawbone devices than on Facebook. Jawbone devices and other activity trackers represent just one category of devices that Wired magazine defines as *lifestyle devices*: "sensors worn perpetually to track personal and biological data that, over time, coalesce to create a portrait of health, habits and behavior."[1] The use of lifestyle devices will continue to rise, which demands that all parties in the research community take notice.

Regulated mobile medical applications (MMAs) are different than mHealth apps and other health care lifestyle devices. Because MMAs are regulated technologies, manufacturers must prove their technologies' safety and efficacy to regulatory agencies. Their technologies are held to further regulatory standards, including regulatory labeling requirements governing any proclamations they make about their MMAs.

What Are Mobile Medical Applications?

The U.S. Food and Drug Administration (FDA) defines mobile apps and MMAs as follows: [2]

> "**Mobile apps** are software programs that run on smartphones and other mobile communication devices. They can also be accessories that attach to a smartphone or other mobile communication devices, or a combination of accessories and software. **Mobile medical apps** are medical devices that are mobile apps, meet the definition [3] of a medical device and are an accessory to a regulated medical device or transform a mobile platform into a regulated medical device."

The FDA's MMA guidance [4] explains that the FDA *does not* intend to regulate all types of MMAs, only a subset of them. To understand the types of MMAs the FDA does intend to regulate, MMAs can be placed into one of three categories.

> **MMAs the FDA will not regulate:** Typically a mobile app used in health care or lifestyle management does not fit the definition of a medical device, in that it does not diagnose, cure, mitigate, treat or prevent a disease in man or animal. The FDA does not intend to regulate these mobile apps. Examples include: electronic medical textbooks or an electronic listing of diseases and conditions; educational tools used for training health care providers or patients; health care office workflow automation tools; and any general purpose tool.

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MMAs for which the FDA intends to exercise enforcement discretion: Sometimes, a mobile app may fit the definition of a medical device, but poses a low risk to public health. The FDA intends to exercise enforcement discretion for this type of mobile app. Examples include: mobile apps and/or devices intended to help patients with certain diagnosed psychiatric conditions to maintain behavioral coping skills; motivational mobile apps; GPS-based mobile apps alerting patients about certain environmental conditions; mobile apps that use gaming technology to improve adherence to physical therapy; and mobile apps that allow patients to send an alert or emergency notification to first responders.

MMAs the FDA will regulate: The FDA will regulate MMAs when they meet the definition of a medical device and pose risks to public safety if they do not function as intended by the manufacturer. Examples include: mobile apps that transform a mobile platform, such as an iPhone, into a regulated medical device with an existing medical device product code; [5] apps that connect to an existing device type for purposes of controlling its operation, function or energy source; and apps that display, transfer, store or convert patient-specific medical device data from a connected device.

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The Life Cycle of a Mobile Medical Application

Simply put, the life cycle of an MMA follows that of a medical device. Life begins at the MMA ideation stage, prompting development of some type of quality system. Regulatory and, ideally, reimbursement strategies are formulated at this stage. A clinical strategy is developed if the FDA requires it and/or if it's necessary to support the reimbursement strategy. Hazard analysis, as part of MMA risk assessment, usability/human factors and software development life cycle considerations can be implemented in parallel with strategy development.

At the verification and validation stage, each software input requirement specification is verified and validated with a "pass" result. Product freeze is then declared. At this point, if the MMA requires a clinical study, an institutional review board [6] submission follows, and the MMA study is initiated upon approval. Data points are gathered and summarized into a regulatory report for submission. Upon a successful submission, a clearance or approval is obtained. The manufacturer may begin marketing and distribution as well as ideation discussions for the next generation MMA.

Sometimes, an iteration of the application may need to be applied during the clinical validation stage. Application software iterations, if they occur during the study stage, must be part of device hazard analysis and documented well.

The key factors for an MMA to achieve a successful life cycle are reimbursement, regulatory and clinical strategies. Today's successful MMAs provide improved clinical outcomes for patients and have demonstrated their value to third-party payers and/or to health care providers to speed and sustain market adoption. Many have used data points derived from randomized, controlled studies to support their clinical and reimbursement claims.

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The Evolution of Mobile Medical Applications — Years 1997 To 2015

MMAs are not new to the FDA. The inaugural MMA, the RhythmStat XL System, was created by Data Critical for a Palm [7] device and cleared as a Class 2 medical device under the 510(k) program in 1997. The RhythmStat XL System telephonically received and recorded electrocardiograph (ECG) data from a cardiac event recorder and transmitted it to a Psion Series 3 [8] palmtop computer, one of the first among the earliest versions of personal digital assistants.

The concept is not new to the greater health care ecosystem either. Since 1997, the health care community has seen MMAs change the way patients and providers think about health care and disease management. An FDA database shows that approximately 50 MMAs were cleared by the FDA between 1997 and 2011. This number has more than doubled since the publication of the MMA Draft Guidance document in 2011.

To date, MMAs are mostly Class 2, follow the premarket notification pathway and are most widely used in chronic disease management, ECG and remote patient monitoring. They have begun to emerge in image diagnostics and medication management/adherence spaces.

MMAs that have achieved widespread market adoption have been successful in tapping into either an existing reimbursement pathway (i.e., one with established coding, coverage and payment mechanisms), or in building a reimbursement pathway. MMAs launching in 2015 and beyond face new reimbursement opportunities and challenges as the current fee-for-service or volume-based reimbursement system slowly shifts to a pay-for-performance or value-based reimbursement system. Additionally, MMAs used in chronic disease management are being purchased directly by third-party payers for use by patients participating in their disease management programs.

Within the last decade, AliveCor, AirStrip Technologies and WellDoc — to name just a few — have successfully navigated the regulatory and reimbursement pathways to develop MMAs that have become game changers in delivering improved health care outcomes.

How Mobile Medical Applications Are Enabling Better Clinical Outcomes

Successful MMAs have proven their value to patients, providers and/or third-party payers by demonstrating improved clinical outcomes and cost-efficient administration. As a result, they have obtained widespread adoption and utilization and deliver sustained revenues to their manufacturers. The following are brief case studies of such MMAs.

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AliveCor: Launched in 2012, the AliveCor Heart Monitor enables health care providers and patients to record, display, store and transfer single-channel ECG rhythms. AliveCor has continuously evolved since its launch, adding new features and mobile operating platforms and obtaining additional FDA-clearances in 2013, 2014 and 2015. The evolved versions are able to display ECG rhythms and detect the presence of atrial fibrillation.

Imagine a patient with a known or suspected heart condition who, under the care of a physician, is able to monitor his/her heart rhythms through the MMA. Also consider a health conscious individual able to simply use the device to monitor exercise-induced heart rates. Now, imagine these individuals being able to use the AliveCor device on a variety of mobile platforms, and not being tied to one (i.e., an iPhone). AliveCor has fulfilled these visions and managed to deliver improved health care management and clinical outcomes to both patients and providers.

Physicians who purchase this technology and/or provide it to their patients can recoup their expenses by billing for the AliveCor Heart Monitor using existing Current Procedural Terminology (CPT) codes. The developer was successful in achieving market utilization by identifying an existing reimbursement pathway that was sufficient to support the physician's use of the technology. Because coding, coverage and payment were already in place, the value of the technology could be demonstrated easily to physicians.

AirStrip Technologies: The core value proposition of AirStrip resides in providing physicians with the ability to monitor patients remotely. Picture a health care campus that includes numerous buildings and floors with operating, examination and other facilities located on different levels or in different buildings. How valuable is it for a physician in that complex to be able to remotely monitor one or all of his or her patients' vital signs in real time? Improved outcomes are achieved by physicians being able to engage with hospitalized patients better and react to unexpected changes in vitals, faster.

AirStrip MMAs have continued to evolve since their launch in 2004 as AirStrip OB. AirStrip OB obtained FDA clearance as a technology used by obstetricians to: rapidly respond to a nurse call regarding fetal heart tracings or maternal contraction patterns by viewing the real-time waveforms remotely on a mobile device such as a PDA or smartphone; proactively review a fetal heart or maternal contraction tracing of a patient in labor and delivery for whom they are unable to be present in the hospital; review the current labor and delivery patient census list; provide a request for remote consultation regarding a fetal heart tracing; and remotely review other real-time numeric data from labor and delivery.

Since 2004, AirStrip has added numerous MMAs. AirStrip launched its data viewing software in 2009; AirStrip RPM in 2010; AirStrip RPM data viewing software and LIFENET Consult in 2012; AirStrip RPM Philips adapter in 2013; and AirStrip RPM remote data viewing software and subsequent modifications in 2015. In total, AirStrip has 11 FDA-cleared MMAs, more than any other manufacturer.

Because health care facilities are the purchasers and users of the AirStrip technologies, traditional reimbursement pathways involving third-party payers are irrelevant. Instead, AirStrip was able to demonstrate to facilities the cost savings and improved patient outcomes achieved through integration of remote patient management.

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WellDoc: WellDoc develops MMAs that function via its diabetes management platform system, a modular platform that can be configured to support health environments ranging from medication adherence to complex multi-disease management. At the system's foundation is a seamless integration of technology, real-time data, analytics, ease-of-use and collaboration — all of which ultimately drive improved metabolic outcomes and reduced health care costs.

Initially predicated on the previously cleared ACCU-CHEK Advisor Insulin Guidance Software and ACCU-CHEK 360° diabetes management system, WellDoc launched the DiabetesManager MMA for over-the-counter use in 2010. The system is indicated for use by health care providers and their adult patients with type 2 diabetes. It captures, stores and transmits blood glucose data. It allows entry of additional diabetes-related health care information and provides coaching and educational information based on blood glucose data and trends, all in real time. By analyzing and reporting blood glucose test results, it supports medication adherence. While not intended to replace the care provided by a licensed health care professional — including prescriptions, diagnosis or treatment — the WellDoc system does a fantastic job of supporting both the patient and provider in chronic disease management.

In 2013, WellDoc launched BlueStar, the first FDA-cleared, mobile prescription therapy for adults with type 2 diabetes. With it, physicians can write prescriptions for BlueStar and those prescriptions will be filled by a pharmacist in the same manner as a drug prescription is filled.

How was WellDoc successful in achieving pharmacy benefits for BlueStar? It proved the value of the technology to health care payers through randomized clinical studies that demonstrated clear clinical and economic benefits to patients. Like AirStrip, WellDoc continues to innovate; it has four FDA-cleared MMAs to date.

MMAs like those manufactured by AliveCor, AirStrip and WellDoc continue to stay ahead of the curve because they are innovative and continue to create value for patients, providers and caregivers by improving clinical outcomes.

Conclusion

Medical device and biopharmaceutical companies are increasingly looking for avenues to innovate and demonstrate improved clinical outcomes. MMAs have, and will continue to provide, an innovative pathway to improve outcomes in chronic disease management, ECG, vital sign monitoring and imaging, among other areas. The opportunities to innovate are plentiful, and manufacturers are beginning to embrace MMAs as part of their clinical development, marketing and business strategies.

About Chiltern

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About Decision Driver Analytics

Founded in 2006, Decision Driver Analytics provides a suite of services that covers the full range of health economics and outcomes research (HEOR) as well as the outreach materials needed to reach investors, health care providers, payers and the public. Utilizing veteran health economists, epidemiologists, biostatisticians, medical writers and reimbursement experts, DDA's services include complete product life cycle value analysis, strategy and planning, clinical economic study services, predictive modeling analytics, definitive analysis studies, communication and sales training.

Appendix: A Summary of the FDA Regulatory Framework for MMAs

The following listing is not comprehensive, but encompasses suggested basic regulatory guidance manufacturers should examine during MMA development. This documentation supports regulatory requirements for the FDA and provides context for understanding the current MMA framework. Requirements for MMA regulatory approval are different for regulatory authorities outside of the U.S. Sometimes, in order to function as intended, an MMA may use a sensor or an activity monitor from which it draws data for further processing. In these cases, the MMA and accessory compose a device system. Depending upon the intended diagnosis or therapy provided, additional guidance documentation and/or standards may need to be examined as part of the reimbursement, regulatory and clinical strategy development.

Guidance Title	Issue Date
Off-the-Shelf Software Use in Medical Devices	September 9, 1999
Submission of Premarket Notifications for Medical Image Management Devices	July 27, 2000
General Principles of Software Validation	January 11, 2002
Cybersecurity for Networked Medical Devices Containing Off-the-Shelf-Software	January 14, 2005
Content of Premarket Submissions for Management of Cybersecurity in Medical Devices	May 11, 2005
Radio Frequency Wireless Technology in Medical Devices	August 14, 2013
Content of Premarket Submissions for Management of Cybersecurity in Medical Devices	October 2, 2014
Medical Device Accessories: Defining Accessories and Classification Pathway for New Accessory Types	January 20, 2015
Mobile Medical Applications	February 9, 2015
Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices	February 9, 2015

1. "Why Jawbone Thinks You'll Still Buy an UP Even if You Have an Apple Watch," WIRED, http://www.wired.com/2014/11/jawbone-thinks-youll-still-buy-even-apple-watch/

2. Mobile Medical Applications, U.S. Food and Drug Administration, http://www.fda.gov/medicaldevices/productsandmedicalprocedures/connectedhealth/mobilemedicalapplications/default.htm

3. Is the Product A Medical Device, U.S. Food and Drug Administration, http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/classifyyourdevice/ucm051512.htm

4. Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff, Feb. 9, 2015, http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf

5. Product codes, developed by the Center for Devices and Radiological Health, are unique and associated with a particular type of device and code of federal regulations. For example, LFR, CGA, NBW and CFR are a few of the product codes associated with glucose test systems under 21 CFR § 862.1345.

6. Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/investigationaldeviceexemptionide/ucm046745.htm

7. The Palm PDA devices were produced by Palm Inc. (then a subsidiary of U.S. Robotics) and launched on March 10, 1997.

8. The Psion Series 3 range of personal digital assistants were manufactured by Psion PLC., the first series of these devices were launched in 1991.

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