

HEALTH LAW, ETHICS, AND HUMAN RIGHTS

Mary Beth Hamel, M.D., M.P.H., *Editor***FDA Regulation of Mobile Health Technologies**

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Medicine may stand at the cusp of a mobile transformation. Mobile health, or “mHealth,” is the use of portable devices such as smartphones and tablets for medical purposes, including diagnosis, treatment, or support of general health and well-being. Users can interface with mobile devices through software applications (“apps”) that typically gather input from interactive questionnaires, separate medical devices connected to the mobile device, or functionalities of the device itself, such as its camera, motion sensor, or microphone. Apps may even process these data with the use of medical algorithms or calculators to generate customized diagnoses and treatment recommendations. Mobile devices make it possible to collect more granular patient data than can be collected from devices that are typically used in hospitals or physicians’ offices. The experiences of a single patient can then be measured against large data sets to provide timely recommendations about managing both acute symptoms and chronic conditions.^{1,2}

To give but a few examples: One app allows users who have diabetes to plug glucometers into their iPhones as it tracks insulin doses and sends alerts for abnormally high or low blood sugar levels.^{3,4} Another app allows patients to use their smartphones to record electrocardiograms,⁵ using a single lead that snaps to the back of the phone. Users can hold the phone against their chests, record cardiac events, and transmit results to their cardiologists.⁶ An imaging app allows users to analyze diagnostic images in multiple modalities, including positron-emission tomography, computed tomography, magnetic resonance imaging, and ultrasonography.⁷ An even greater number of mHealth products perform health-management functions, such as medication reminders and symptom checkers, or administrative functions, such as patient scheduling and billing.

The volume and variety of mHealth products

are already immense and defy any strict taxonomy. More than 97,000 mHealth apps were available as of March 2013, according to one estimate.⁸ The number of mHealth apps, downloads, and users almost doubles every year.⁹ Some observers predict that by 2018 there could be 1.7 billion mHealth users worldwide.⁸ Thus, mHealth technologies could have a profound effect on patient care.

However, mHealth has also become a challenge for the Food and Drug Administration (FDA), the regulator responsible for ensuring that medical devices are safe and effective. The FDA’s oversight of mHealth devices has been controversial to members of Congress and industry,¹⁰ who worry that “applying a complex regulatory framework could inhibit future growth and innovation in this promising market.”¹¹ But such oversight has become increasingly important. A bewildering array of mHealth products can make it difficult for individual patients or physicians to evaluate their quality or utility. In recent years, a number of bills have been proposed in Congress to change FDA jurisdiction over mHealth products, and in April 2014, a key federal advisory committee laid out its recommendations for regulating mHealth and other health-information technologies.¹² With momentum toward legislation building, this article focuses on the public health benefits and risks of mHealth devices under FDA jurisdiction and considers how to best use the FDA’s authority.

CLINICAL UTILITY AND RISKS
OF MHEALTH

Collectively, mHealth products hold the promise of improving health outcomes, reducing medical errors, avoiding costly interventions, and broadening access to care. Leading voices from the medical,¹³ government,^{10,11,14} financial,¹⁵ and technology¹⁶ sectors have endorsed the idea that

mHealth can transform American medicine. Currently, the Department of Health and Human Services lists several federal mHealth initiatives.¹⁷ For example, the Department of Veterans Affairs developed an app to help veterans with post-traumatic stress disorder,¹⁸ and the National Institutes of Health offers an app that calculates body-mass index.¹⁹ There are three ways that mHealth's potential could be realized.

First, some mHealth products, such as the above-mentioned diabetes and cardiology apps, aim to improve the quality of care and reduce medical errors by gathering more data on patients more frequently and using that data more effectively. Enhanced monitoring, for example, might help prevent acute episodes or manage chronic conditions.¹⁻⁶ Many mHealth products integrate clinical-decision support — software algorithms that use patient-specific data to make customized diagnoses or treatment recommendations. Instant wireless communication might also allow providers to better coordinate care and thus reduce duplication and mistakes.

Second, many mHealth products, such as those that help monitor chronic conditions, might reduce spending by eliminating unnecessary hospital or physician office visits. Such technologies might also help to avoid duplicative procedures by integrating electronic health records, or simply save on administrative costs, through streamlined scheduling and billing, for example. In a recent demonstration, a health plan saved 8.8% in spending with a diabetes program that used text messages to remind patients to check their blood sugar levels and refill prescriptions.²⁰

Third, many mHealth technologies could broaden access to care, either by extending the reach of providers through remote monitoring of patients or by giving advice when users otherwise would not visit a medical professional. Apps like Pocket Doctor and iTriage, which suggest possible diagnoses on the basis of inputs from patients, are proliferating. Making medical advice available beyond traditional settings could broaden access to care for the uninsured, those living in rural areas, immigrants, and perhaps even elderly patients. Indeed, mHealth technologies are already being deployed to expand access to care in less developed countries.²¹

But to reach their transformative potential, mHealth technologies must be safe and effective.

Although the vast majority of mHealth products are very low-risk, new evidence emerging through independent evaluations reveals products that do not work as claimed or that make mistakes.²²⁻²⁵ In 2011, Pfizer sent a Dear Doctor letter warning that its Rheumatology Calculator app was generating mistakenly high and low scores for measuring tender and swollen joints in patients with arthritis, sometimes by as much as 50%.²⁶ The letter warned physicians to delete the app and review its calculations. In 2012, Sanofi Aventis recalled its diabetes app because it was miscalculating insulin doses, which might lead to “dangerously low or high blood glucose levels in diabetic patients.”²⁷ Broader reviews show mHealth apps that make claims lacking scientific support, are designed without the input of a medical professional, or even contravene evidence-based guidelines.²²⁻²⁵ Some apps simultaneously promise medical benefits while disclaiming that the app is for entertainment purposes only. For example, the app Pocket Doctor Lite, which purports to provide “diagnosis by body area,” included a disclaimer on the iTunes Store that “Pocket Doctor cannot guarantee the accuracy of the diagnoses. You use it at your own risk.”²⁸

Increasing reliance on mHealth raises questions about compromised patient privacy, the cross-jurisdictional practice of medicine, and legal liability for injuries.²⁹ Serious mistakes with an mHealth product might affect thousands of patients at a time and often without ready mechanisms for detection and correction. Although other federal agencies — particularly the Federal Communications Commission (FCC) and the Office of the National Coordinator for Health Information Technology — have authority over the broader universe of mHealth products, public health oversight over riskier products primarily falls on the FDA.

THE FDA'S EMERGING REGULATORY FRAMEWORK FOR MHEALTH

The FDA's jurisdiction over medical devices gives it jurisdiction over many, though far from all, mHealth technologies. The Food, Drug, and Cosmetic Act (FDCA) defines a “device” as including instruments and objects intended to diagnose diseases or other conditions or intended to cure, mitigate, treat, or prevent diseases, including any

components, parts, or accessories.³⁰ Thus, the FDA has authority over mHealth products that perform core medical functions, such as providing direct diagnosis or treatment, or making diagnostic or treatment recommendations.

In a nonbinding guidance document, the FDA explained that it would focus on the intended functionality of mHealth products, not their mobile platforms.³¹ Thus, the FDA intends to oversee “only those mobile apps that are medical devices and whose functionality could pose a risk to patient safety if the mobile app were to not function as intended.”³¹ The FDA cites several examples, including apps that perform electrocardiography or electroencephalography, apps that measure eye movements to diagnose balance disorders, apps that act as wireless remote controls for computed tomography, and apps that control implantable neuromuscular stimulators. The FDA calls these “mobile medical applications.” The agency does not propose to regulate phone or tablet manufacturers themselves. The FDA explained that it will use its discretion to not enforce agency requirements against apps that technically qualify as “devices” but pose a lower risk. Examples include apps that help users track asthma attacks and inhaler use, symptom checkers, and behavioral-modification apps for users with psychiatric conditions. This discretionary category leaves a considerable gray area between products that clearly must be regulated to ensure safety and those that pose little or no risk to patients.

The FDA can review mHealth devices through the FDCA’s device-review process.³² Congress created three classes of devices on the basis of their risks: class I (low risk), class II (moderate risk), and class III (high risk).³² To market a new class III device, the FDA generally requires manufacturers to submit a premarket-approval application, which usually involves collecting clinical data showing that the device is safe and effective for its intended uses.^{32,33} By contrast, the FDA allows manufacturers of most class II devices to file a much less burdensome notification, as outlined in Section 510(k) of the FDCA (also known as premarket notification), in which the manufacturer declares that its device is “substantially equivalent” to a previous device.³⁴ Most class I devices are exempt from even this requirement.³⁵

The FDA has cleared approximately 100 mo-

bile medical applications for marketing,²⁷ all through the 510(k) pathway.^{36,37} For example, in 2009, the FDA cleared an app that allows obstetricians to remotely monitor labor and delivery, including fetal vital signs.³⁸ In 2011, the FDA cleared an app that allows providers to view medical images on smartphones and tablets.⁷ The sole class III device was electrocardiograph software, cleared by the FDA in 2002 through the 510(k) pathway, that connected a 12-lead cable to a personal digital assistant, the precursor to smartphones.^{39,40} The FDA later downclassified this device to class II.⁴¹ Still, far more low-risk mHealth products will receive no premarket review at all because they fall into the discretionary category of exempt products, according to FDA guidance.³¹

Once an mHealth device is on the market, the FDA reviews adverse events reported by manufacturers and can recommend market withdrawals or changes to the labeled indication.⁴² Some mHealth products are beginning to appear in the FDA’s reporting database.⁴³ A search of this database for adverse events related to just one diabetes app (iBGStar) returned 52 reports from 2012 through early 2014. The FDA also reviews promotional messages to ensure they are consistent with the product’s regulatory authorization. In 2013, the FDA warned the company Biosense that it was marketing its urine-analyzer app without FDA clearance.⁴⁴ Biosense had been selling its app on the iTunes Store for \$19.99, with a disclaimer that it was not an FDA-regulated device, despite statements on its website that the app could help users “understand and manage diseases like diabetes, . . . urinary tract infections, and pre-eclampsia.”⁴⁵

The challenge of adapting the FDA’s device framework to mHealth has parallels to the recent controversy between the FDA and 23andMe, a private company that provides personalized genetic-testing services. An FDA warning letter to the company⁴⁶ generated a considerable amount of criticism and confusion about the proper scope of the FDA’s authority and whether such authority should apply to new products such as consumer genetic testing.⁴⁷ Similarly, the proliferation of mHealth products has pushed the FDA to reconsider how mobile software fits into its regulatory framework. For example, although many mHealth products are new and thus might be candidates for more rigorous premarket ap-

proval, almost all apps have been cleared as being “substantially equivalent” to previous devices under the 510(k) process.²⁷ Thus, the FDA is clearing apps that are “substantially equivalent” to predicate devices, even when the predicate has very different technological characteristics⁴⁸ and was developed well before smartphones or apps even existed. App developers, many of whom are unaccustomed to regulation, complain that even the 510(k) process is too long,⁴⁹⁻⁵¹ even though the FDA reports that the average total time from a 510(k) submission to a decision by the FDA is only 110 days.³⁷

The FDA’s postmarketing requirements also do not apply neatly to mHealth. For example, the FDA’s quality system regulation does not easily accommodate mobile software that can be frequently updated and adapted to new uses. Certain quality requirements, such as production and process controls,⁵² apply to hardware but not software devices.³¹ Moreover, the software-industry practice of releasing “beta” versions to solicit user feedback can be problematic when FDA regulations require that testing of investigational devices be overseen by an institutional review board and that informed consent be obtained.⁴⁵ There is also uncertainty over who is responsible for product-labeling updates, adverse-event reporting, and cybersecurity among parties in a complex supply chain that can include multiple software developers.^{31,53}

RECENT REFORM PROPOSALS

In light of ongoing regulatory challenges, the FDA and Congress are considering more tailored approaches. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA)

directed the FDA, FCC, and the Office of the National Coordinator for Health Information Technology to recommend a “risk-based regulatory framework for health information technology, including mobile medical applications, that promotes innovation, protects patient safety, and avoids regulatory duplication.”⁵⁴ The recommendations, published in April 2014, propose separating products into three categories: products that perform “administrative” functions, such as billing and practice-management software; products that perform “health management” functions, such as medication management and “most clinical decision support”; and products that perform “medical device” functions.¹² The recommendations would limit FDA oversight to products in this final category (Table 1).

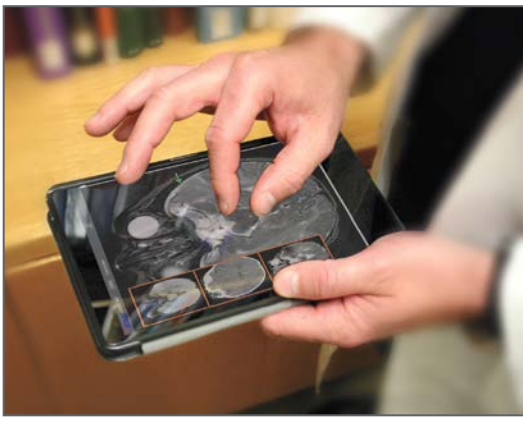
Although the FDASIA report suggests steps that the FDA can take to clarify its oversight of mHealth, a series of bills proposed in Congress suggest growing momentum toward legislation. For example, a bill that was proposed in 2012 and reintroduced in 2013 would create a new Office of Wireless Health Technology within the FDA to help facilitate approval of mHealth products and dedicate slightly more FDA resources to the area, without giving the FDA any new authority.^{55,56} But a restrictive bill, introduced in October 2013, would preclude the FDA from regulating “clinical software,” which includes clinical-decision-support programs.⁵⁷ A third bill, proposed in February 2014 in the Senate, also would exclude “clinical software” from FDA regulation.⁵⁸

Many mHealth products incorporate clinical-decision support, such as drug-dose calculators or symptom checkers. Under the October 2013 bill, even software that uses patient data and

Table 1. Jurisdiction of the FDA over Products Used in Health-Information Technology.*

Function of Products	Examples of Products	FDA Jurisdiction
Administrative	Billing software, claims software, scheduling software	No, since functions do not meet the definition of a “device”
Health management	Provider order-entry software, medication-management products, data-capture and clinical-encounter-management software, most clinical-decision-support tools	Possibly, since functions might meet the definition of a “device,” but they are seen as low-risk and subject to discretion for FDA enforcement
Medical device	Mobile medical apps, medical-device accessories, high-risk clinical-decision-support tools	Yes, since functions meet the definition of a “device”

* Product categories are based on the taxonomy of health-information-technology products proposed in the Health IT Report.¹²



recommends a “course of clinical action” would not be regulated by the FDA if it was intended for use only by health care providers in health care settings or if it “does not directly change the structure or any function of the body.”⁵⁷ The FDASIA report also recommends limited FDA oversight over clinical-decision support, which would be restricted to products such as computer-aided detection software or radiation-treatment-planning software that present higher risks.¹² Both approaches would provide scant oversight to products that might evolve into some of the more innovative and important mHealth products in the near future. If health care providers or institutions rely on such products to cut spending or make more effective clinical decisions, it is crucial that the algorithms are safe and work as intended — the twin goals of FDA oversight.

POLICY RECOMMENDATIONS

A common concern driving legislation that would reconsider the FDA’s role is that many members of Congress and industry believe that regulation will stifle mHealth innovation. The true challenge, however, is creating a regulatory framework that encourages high-value innovation while also preventing the market from being overcome with products that are ineffective or unsafe.⁵⁹ The FDA’s premarket and postmarket authorities are essential to these goals. If Congress passes legislation, it should update the FDA’s authority to better fit mHealth and preserve the FDA’s discretion to address emerging risks.

One important step is to avoid narrowing the FDA’s jurisdiction. Recent bills would limit the

agency’s jurisdiction by removing FDA oversight over certain types of clinical-decision support software but not others.^{57,58} Although to some observers such proposals may appear to be designed to protect discretion in the practice of medicine, we think they put doctors in a more precarious position. Without the rigors of FDA oversight, it will be harder for them to trust the advice their devices give them. Moreover, the creation of precise statutory definitions for FDA jurisdiction over mHealth products risks anchoring the authority of the FDA to existing products, which could create problems for future technologies. The FDA should continue to be able to apply its authority to new, potentially risky mHealth products that perform the functions of medical devices.

Indeed, we think the FDA should regulate mHealth products that incorporate clinical-decision support. Although the FDA has been unclear about precisely which clinical-decision-support products it regulates,⁴⁵ recent bills would create even more confusion by differentiating products that directly affect the structure or function of the body from those that do not, and products marketed for use by health care professionals in health care settings from those that are not.^{57,58} The FDASIA report calls on the FDA to regulate only clinical-decision-support products that present increased risks at the same time that it solicits public comments on how to draw that distinction.¹² Nevertheless, recent experience suggests that mobile products incorporating clinical-decision support will become more commonplace and ambitious.

We also believe that the FDA should update earlier guidance on how its quality system regulation applies to software.⁶⁰ Congress might consider permitting third-party validation of the underlying algorithm and other quality safeguards tailored to mHealth, as recommended by the FDASIA report. But any private standards and best practices would have more traction if the FDA retained discretion to enforce blatant safety lapses. Moreover, the FDASIA report does not address deficiencies in the FDA’s current device framework, including its reliance on the 510(k) pathway for mHealth products without genuine predicates.

A more radical approach could involve congressional creation of a unique approval pathway and postmarketing-surveillance system for

mHealth products and other types of medical software. Shoehorning such products into the 510(k) pathway is problematic — on the one hand, consumers may not be reassured by FDA-cleared software products that are both completely new and yet also “substantially equivalent” to previous products. On the other hand, it seems inefficient for app manufacturers to submit repeated applications for each update or change akin to manufacturers in the far less rapidly evolving field of implantable hip prostheses. The FDASIA report highlights the need to clarify the process for software modifications. Although the FDA has published guidance on premarket submissions for software products,⁶¹ Congress should push the FDA to rethink this framework for mobile software. One model could be premarket review that brings lower-risk mHealth products to market more efficiently but only if manufacturers gather postmarketing data on the safety and effectiveness of the product, perhaps with a mandatory reevaluation period by the FDA or an analogous license-renewal requirement. Though conditional approvals have had a relatively poor track record in the prescription-drug area and can be resource-intensive for the FDA, such a pathway may both encourage timely innovations and generate better data to support them.

When considering such reforms, Congress must recognize that FDA resources are not growing commensurate with the number of mHealth products in its jurisdiction. These resources are essential to support enforcement actions against noncomplying mHealth products, consistent with the FDA’s final guidance.³¹ With potentially thousands of mHealth products under the FDA’s domain, agency authority will be undermined if the FDA cannot enforce its requirements. The agency needs additional funding and in-house technical expertise to oversee the ongoing flood of mHealth products. One possibility would be to fund additional oversight through an approval fee on mHealth products, similar to the user fees for drugs. As experience with the dietary-supplement market has shown,⁶² manufacturers will have few incentives to comply with FDA requirements that lack enforcement teeth.

To coordinate its efforts, the FDA may need a dedicated center or office to regulate mobile applications and other device software. The charge of this new entity might be even broader than

that outlined for the Office of Wireless Health Technology in previous legislation, which focused only on wireless software.^{55,56} A dedicated center would also help to build regulatory capacity for a future that will be much more digitized than it is even now. The FDASIA report recommends the establishment of a Health IT Safety Center, which would not have regulatory authority, would reside outside the FDA, and would serve primarily to disseminate best practices.¹²

As mHealth products become more ubiquitous and ambitious, targeted FDA oversight will help to protect the public health, sustain consumer confidence in mHealth products, and encourage high-value innovations. The FDASIA report envisions a modest role for the FDA. In our view, Congress must recognize that robust FDA oversight is not necessarily incompatible with innovation in the mHealth industry. In fact, the industry’s long-term potential may depend on it.

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