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Digital Medicine

A transformative digital health technology

Author: Michael Campbell, Medical Technology Risk Control

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Executive Summary

Digital medicine is an emerging technology which is likely to have an immensely disruptive influence on the medical device market.[1] It is central to the concept of digital health, a confluence of genomics, proteomics, metabolomics, epigenomics, and biomarkers, which are enabling us to know human biology on an individual basis.[2] These new digital tools are capable of recording clinical data and generating medical information, and make it possible to develop digital medicine that is more precise, effective and widely distributed than current medical practices.[3] While digital medicine first emerged a few years ago as wearable devices, the newest generation of ingestible electronics will allow practitioners to diagnose, detect and monitor physiological conditions across a wide range of diagnostics and therapeutics.

Ingestible Electronics

The key to the next generation of digital medicine is the ingestible sensor, a device which looks like an ordinary encapsulated pill that contains sensors and communication capabilities that allow it to be monitored for various physiological variables it is intended to detect.[4] Patients swallow the pill as they would any therapeutic, and upon ingestion the device will begin sending data on those parameters it is designed to identify.[5]

Companies such as Samsung and Apple have historically been among the leaders in emerging digital health trends such as wearables and mobile technologies and applications designed to detect and report personal health data[6]. However, it has been medical device (companies?), manufacturing start-ups, and even universities and research institutions that have been leading the development of digital medicine. For example, in 2015 the U.S. Food and Drug Administration (FDA) accepted the first digital medicine application for an ingestible device – a "sensor-enabled tablet" designed to measure a patient's vital signs as well as that patient's adherence to prescription medication schedules.[7] The device, on activation by the patient's stomach acid, transmits data to a patch worn on the patient's skin. This data can then be read by medical practitioners.[8] This technology is being developed as a means of monitoring patient adherence to medication regimens during clinical study of new therapeutics, as patient compliance or noncompliance with therapeutic regimens can have critical consequences on the outcomes of clinical trials.[9]

Another device is an ingestible sensor designed to monitor a patient's core body temperature in real-time, which can also be used on groups of patients undergoing clinical study.[10] The Massachusetts Institute of Technology has been active in this emerging field, having developed an ingestible sensor that is designed to monitor vital signs[11].They have also developed a device encapsulated within an ice-cube pill, which when ingested transforms into a miniature robot capable of retrieving accidentally swallowed foreign objects, patch wounds, and even deliver medications to specific areas within the gastrointestinal tract.[12]

Large technology companies such as Google and Motorola are even exploring the use of ingestible electronics outside the realm of digital medicine, envisioning their use as an individual "authentication token," which can verify a person's identity and communicate with devices outside the person's body.[13]

Digital medicine is only beginning to emerge as a major subset of digital health, but there are early signs that it will represent a significant breakthrough. For example:

- Novartis (a global healthcare company) has partnered with Qualcomm (a leader in next-generation mobile technologies) to form a partnership that has established $100M in venture capital funding towards digital medicine technology development.[14]
- Proteus Digital Health is a pioneer in digital medicine and developer of an ingestible sensor designed to record adherence to prescription medication regimens and to collect and transmit data on physiologic metrics like heart rate, physical activity and rest. They have secured an additional $50M in investments to further develop their platform.[15]
- Akili Interactive Labs is a company developing a digital medicine technology platform for the evaluation and treatment of a range of disorders including pediatric attention deficit hyperactivity disorder (ADHD), autism spectrum disorder, depression, Alzheimer's disease and traumatic brain injury. They received $30.5M in new equity investment at the beginning of 2016.[16]

Digital medicine has also caught the attention of the Obama administration, with the President recently submitting an op-ed to *The Boston Globe* announcing investments and partnerships by the National Institute of Health with research institutes across the country in the field of "precision medicine," a field in which digital medicine technology acts as an important diagnostic and data gathering tool.[17]

Regulatory Considerations

The FDA appears to be taking a precautionary approach to approval of ingestible sensors. In September 2015, the FDA accepted the first digital medicine New Drug Application (NDA)[18], but later rejected the NDA and in April 2016 issued a Complete Response Letter (CRL) requesting additional information from the

applicant. This included data on the device's performance in expected use conditions, as well as additional human factors testing.[19]

The FDA has been in front of the emergence of ingestible digital medicine technologies. As far back as 2001, it reclassified an ingestible sensory device from Class III to Class II and issued special controls guidance for a specific device intended to image the gastrointestinal system.[20] The FDA has since established an Emerging Technology Team, and in 2015 issued draft guidance on emerging technologies in pharmaceutical manufacturing.[21] It has also provided presentations in public forums that included addressing the emergence of digital medicine.[22]

More recently, the FDA released guidance which moves towards standardization for evaluation of the biocompatibility of medical devices. They are citing ISO 10993-1 as a governing standard that applies to the general and test-specific evaluation of medical devices.[23] This is likely to have a direct influence on the device's modes of action, and the choice of materials used in the construction of ingestible devices.[24]

Other Concerns

A number of concerns have been expressed by regulatory authorities and many independent institutions relative to unintended consequences of the use of digital medicine.

- Privacy - Foremost among these is the matter of data privacy. Advocates of the technology claim that potential privacy risks have been thoroughly evaluated, but also express concern that personal health information could wind up in the hands of third parties such as health insurance companies.[25] Insurance companies could gain access to data from these devices and infer on a patient's specific illness or disorder and limit or deny coverage on that basis. Also, as with any type of PHI data, there are data security issues that need to be considered.
- Limited Time Window - From a data gathering perspective, the benefit of ingestible devices has also been questioned since these devices only remain in the body for about twenty-four hours. In order to obtain consistent data or make the device more useful, means of extending their time in the body should be explored.[26]
- Doctor-Patient Interaction - Some have expressed concern that the technology may "remove doctors from the equation" of patient care and result in less control over the quality of the data generated by the devices.[27] For example, data may be generated by a device that is not approved by the doctor or one that the doctor does not trust, and may result in the doctor repeating the test.

The FDA has also expressed some concerns about ingestible devices and has begun recommending regulatory considerations such as:

- Developing failure modes analysis evaluation as this is currently expected of most any other medical device brought to market.
- Requiring that data be collected for both clinical study and post-market, "in-vivo" performance of the devices. This will allow device manufacturers to compare and contrast the performance of the devices in clinical environments versus that experienced in "real world" use.[28]

Conclusion

The recent digital health revolution brought health and wellness to a personal level through wearable and mobile devices equipped with applications that allow individuals to track their own personal health information. The more recent emergence of the digital medicine, combined with advances in microelectronics including miniaturization, reduced power consumption and improved efficiency are leading to ingestible electronics that provide real-time monitoring of patient data across a broader range of physiological factors. These new tools can provide medical practitioners with powerful resources that will allow them to define patient health at unprecedented levels, with goals of disease prevention and preservation of health. These advances in digital health and the emergence of digital medicine may be a transformative force in the evolution of the medical device market and healthcare in general.

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To learn more about how OneBeacon Technology Insurance™ can help you manage online and other technology risks, please contact Dan Bauman, Vice President of Risk Control for OneBeacon Technology Insurance at dbauman@onebeacontech.com or 262.966.2739.

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