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The FDA's Digital Health Software Precertification (Precert) Program

Despite being a world leader in the development of digital health technologies, developers in the US are often apprehensive about the often long and detailed process of the Food and Drug Administration's ('FDA') premarket certification review. The FDA's new Digital Health Software Precertification (Precert) Program ('Precert Program'), announced in August 2017, seeks to pilot a 'fast-track' process for software as a medical device ('SAMD') developers that the FDA trusts to produce consistently high quality, safe and secure products, removing the necessity to undergo the full review process for each product produced. Jeffrey K. Shapiro, Director at Hyman, Phelps & McNamara, provides background to and discussion of the FDA's review processes and its new Precert Program, and considers the impact the Precert Program may have on the digital health market.

Medical devices began incorporating software several decades ago. This use of software has taken two forms. The first is 'software in a medical device' ('SIMD'), in which a traditional medical device incorporates software to aid functionality. An example might be robotic surgical platforms that incorporate sophisticated software controlled navigation features.

The second form is SAMD, in which the software itself is the medical device. An example might be a software product that analyses lung x-rays and highlights potentially cancerous lesions for the radiologist (i.e., computer assisted diagnosis, or 'CAD').

In recent years, SAMD has exploded as a category - to the point that it has a new name: 'digital health.' There has been widespread development of Big Data, machine learning, wearables, cloud based and mobile healthcare applications - all aimed at assisting physicians and patients in the healthcare space.

A key challenge for digital health has been the FDA's premarket review requirements. In general, they are expensive and slow. The burden is not simply the FDA's review time, but also the time spent by firms seeking to understand the FDA's requirements, gathering necessary data, preparing voluminous submissions and answering the FDA's questions.

The traditional medical device industry, including devices with SIMD, has learned to work within these constraints and remain profitable. Nonetheless, everyone should understand that innovation in the medical device industry, almost by definition, is much slower than it would be in a world without the FDA's premarket review. It is generally thought (albeit without much empirical analysis) that this trade off is a favourable one, insofar that it ensures that devices come to market with a significantly greater degree of assured safety and effectiveness than would otherwise be the case.

The digital health medical device industry may have difficulty remaining financially viable within the traditional regulatory structure. Not only does digital health iterate faster, but it likely needs to do so in order to become established. At present, the technology is expected to greatly improve healthcare, but that remains to be seen in practice. For now, the industry must have the flexibility to try new applications, to improve those that seem to add value and to iterate away from those that do not. If the digital health sector cannot move forward quickly enough to become established and profitable, the financing may eventually dry up or the firms with deep pockets (e.g., Apple)

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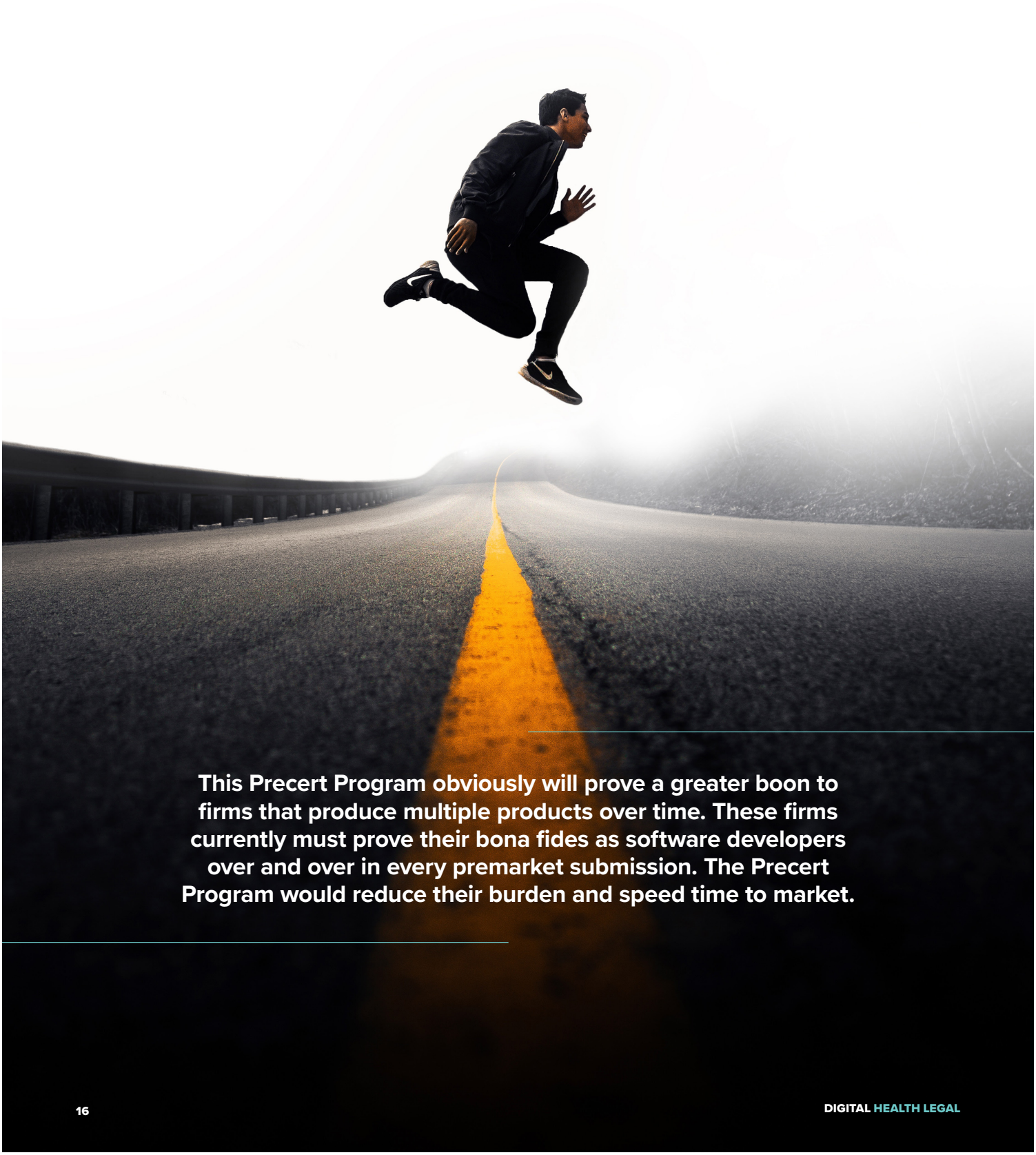

This Precert Program obviously will prove a greater boon to firms that produce multiple products over time. These firms currently must prove their bona fides as software developers over and over in every premarket submission. The Precert Program would reduce their burden and speed time to market.

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may move on to greener pastures. It appears that the FDA under the current administration is cognizant of this situation. Thus, last July, the FDA's new Commissioner stated the following:

"FDA's traditional approach to medical devices is not well suited to these [digital health] products. We need to make sure our approach to innovative products with continual updates and upgrades is efficient and that it fosters, not impedes, innovation. Recognizing this, and understanding that the potential of digital health is nothing short of revolutionary, we must work toward establishing an appropriate approach that's closely tailored to this new category of products. We need a regulatory framework that accommodates the distinctive nature of digital health technology, its clinical promise, the unique user interface, and industry's compressed commercial cycle of new product introductions[1]."

To move forward in line with this announcement, the Center for Devices and Radiological Health ('CDRH') on the same day issued a 'Digital Health Innovation Action Plan[2].' The interesting thing is that many CDRH actions have involved getting out of the way, i.e., identifying categories of software that do not require regulatory oversight even though they could fit within the broad statutory definition of a medical device. For instance, the plan reminds everyone:

- The FDA focused its oversight on mobile medical apps to only those that present higher risk to patients, while choosing not to enforce compliance for lower risk mobile apps;
- It confirmed its intention to not focus its oversight on technologies that receive, transmit, store or display data from medical devices; and
- It chose not to focus its oversight on products that only promote general wellness.

Congress also has weighed in on the FDA's oversight of digital health. The recent 21st Century Cures Act has a software provision (Section 3060) that statutorily defined the categories of digital health software that the FDA shall not regulate. The one that had been the most uncertain was clinical decision support software ('CDSS') for physicians. This category (with certain exceptions) can now move forward without the burden of FDA premarket review.

There remains the question about how to regulate SAMD that is validly subject to FDA premarket review. Here, the problem is that the FDA's approach to the premarket review of software is long in the tooth, and was developed for SIMD and not SAMD. One can glean a sense of the obsolescence of the FDA's guidance by typing 'software' into the FDA's guidance document search engine (with 'final' guidance as a filter). Of 4,171 entries, there are only seven guidance documents with 'software' in the title.

These are the classic guidances that typically apply when one is preparing a premarket submission. With a few exceptions not pertinent to actual preparation of premarket submissions, the dates range from 1987 to 2005. During this earlier time period, the FDA's primary concern was the movement of traditional medical device companies toward incorporating software into their products (i.e., SIMD). Since the firms were new to software, the FDA naturally (and through experience) did not fully trust them to design and test software properly.

For instance, the guidance on software validation[3] and the guidance on the content of premarket submissions for software are the primary instruction from the FDA on the software portion of premarket submissions. These guidances, issued in 2002 and 2005 respectively, require information that essentially enables the FDA to review the design and testing of the software. The degree of required software documentation and FDA review varies (based on whether the software is deemed to be of minimal, moderate or major level of concern). In each of these cases, however, the FDA is effectively reviewing the quality of the software in addition to the clinical safety and effectiveness of the device when the software functions as intended. This added quality review has significantly burdened both industry (which must supply the documentation) and agency (which must review the documentation).

15 years on, and this approach seems especially outdated when applied to digital health firms. For one thing, the process of designing and testing software has also greatly improved in the interim. Additionally, digital health firms are built specifically to develop software and can be expected to know how to design and test it (or they will not last long). Most importantly, the current FDA approach to premarket review is not nimble enough for the fast level of iteration that the digital health industry is likely to need.

What is to be done? The FDA now proposes to balance the competing considerations of development speed with minimisation of patient risk by adopting the Precert Program. As described by the Commissioner[4], the Precert Program is intended to develop "criteria [that] can be used to assess whether a company consistently and reliably engages in high-quality software design and testing (validation) and ongoing maintenance of its software product." Firms meeting these criteria could eventually "bring certain types of digital health products to market without FDA premarket review or after a streamlined, less burdensome FDA premarket review."

This idea is very interesting, because it could enable the FDA to develop trust in the design and testing of the software up front, and then focus more on clinical performance considerations in product review. That may be a viable way to shorten the review cycle and reduce the burden. It would allow a firm to prove to the FDA in advance that its software 'manufacturing' is robust.

At the same time, if a firm has not obtained precertification, the FDA can require full detail as to the design and testing of its software. This Precert Program will obviously prove

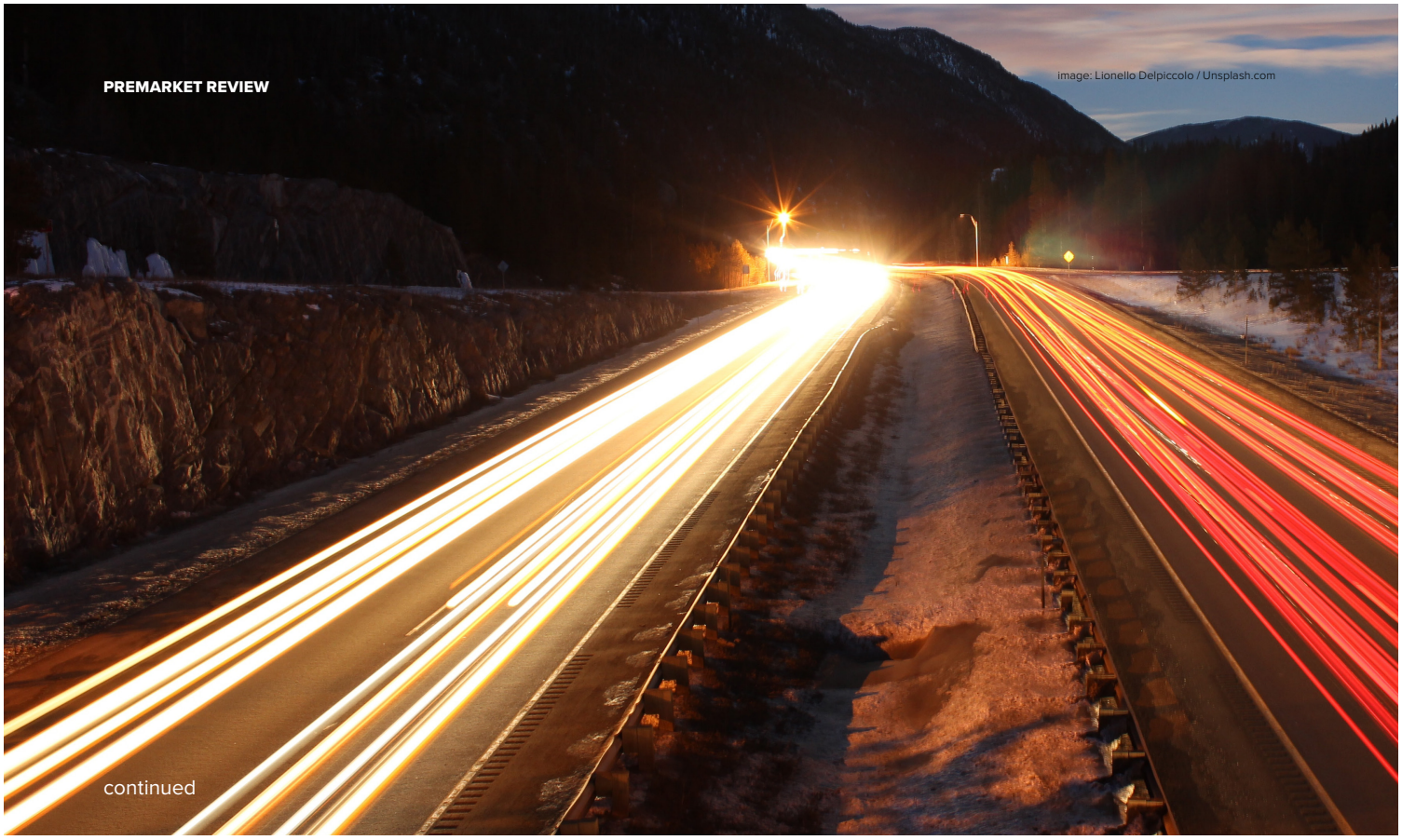

image: Lionello Delpiccolo / Unsplash.com

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a greater boon to firms that produce multiple products over time. These firms currently must prove their bona fides as software developers over and over in every premarket submission. The Precert Program would reduce their burden and speed to market.

The Precert Program does seem to be moving forward on schedule. On 26 September 2017, the FDA Commissioner announced the first participants:

- Apple, Cupertino, California;
- Fitbit, San Francisco, California;
- Johnson & Johnson, New Brunswick, New Jersey;
- Pear Therapeutics, Boston, Massachusetts;
- Phosphorus, New York, New York;
- Roche, Basel, Switzerland;
- Samsung, Seoul, South Korea;
- Tidepool, Palo Alto, California;
- Verily, Mountain View, California.

Obviously, these companies are all well known and reputable names. Presumably, they can help the FDA learn to identify the key elements of a robust, high quality software development program. In this regard, however, the FDA could be criticised for not selecting for comparison at least a few companies with unknown software quality and/or known bad software quality. It helps to know both sides of the equation in order to calibrate a screening program. In announcing this selection[5], the FDA underscored its intent that the Precert Program will help formulate the screening criteria to be used: "With the information gleaned through the pilot program, the agency hopes to determine the key metrics and performance indicators for precertification and identify ways that precertified companies could potentially submit less information to the FDA than is currently required before marketing a new digital health tool as part of a formal program."

At least that is the hope. The devil will be in the details. Specifically, the FDA must develop criteria for precertification that are not overly burdensome (e.g., based upon setting up bureaucracies and procedures that only large firms can afford) but which minimise the risk of certifying a firm that actually is not very good at developing software. A substantial error in either direction could doom the Precert Program. If the criteria require too much internal bureaucracy (focusing on process rather than outcomes), then only large firms like an Apple or a Johnson & Johnson will likely qualify. On the other hand, if the criteria do not screen out bad software developers, the FDA may end up unwittingly clearing a series of software products that are badly designed or tested. Developing screening criteria that strike the right balance will be easier said than done. Because of the general tendency of bureaucracies to create the world in their own image, it seems likely that the former type of error (being overly focused on process rather than outcomes) is the more substantial risk. A pertinent example of the FDA's focus on process is the Quality System Regulation (21 CFR Part 820) ('QSR'), which has been applicable to medical device manufacturing since 1996. It is a regulation that is focused almost exclusively on procedures and documentation, and not product quality *per se*. There has been little analysis in the ensuing 20 years as to whether the QSR is actually responsible for significantly improving and maintaining the safety and effectiveness of medical devices, and much less of whether any of it is cost effective.

One reason these questions are ignored is that the US Congress long ago mandated implementation of the QSR by statute, so the worth of this regulation does not need to be proved; it is the *status quo* and would be difficult to change. Most analysts simply assume that it is a key element of device safety and effectiveness. In contrast, the FDA's Precert Program will not be mandatory, but will offer the 'carrot' of faster and easier premarket review. We will know quickly if it is overly burdensome if few firms are participating after the Precert Program gets beyond the pilot stage. One point not raised by the FDA to date is the potential applicability of the Precert

1. https://blogs.fda.gov/fdavoice/index.php/2017/07/fda-announces-new-steps-to-empower-consumers-and-advance-digital-healthcare/
2. https://www.fda.gov/downloads/MedicalDevices/DigitalHealth/UCM568735.pdf
3. https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085281.htm
4. https://blogs.fda.gov/fdavoice/index.php/2017/07/fda-announces-new-steps-to-empower-consumers-and-advance-digital-healthcare/
5. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm577480.htm

One point not raised by the FDA to date is the potential applicability of the Precert Program to SIMD.

Program to SIMD. Today, medical device companies are much more sophisticated about incorporating software into their devices. Pursuant to the ancient 2002 General Principles of Software Validation, these companies continue to produce a great deal of documentation that may no longer be necessary for FDA to review.

No doubt, SIMD is not as new and sexy as SAMD. Nonetheless, if the Precert Program does prove a success, the FDA should strongly consider extending it to SIMD. Doing so may result in even greater time savings for the agency, because it probably reviews more SIMD than SAMD. It is also past the time to update the 2002 guidance and other guidance generally applicable to premarket review of SIMD.

What's next for the Precert Program? The FDA intends to hold a public workshop in January 2018 to report on and review initial findings. The goal is to inform product developers who are not participating in the Precert Program, so they can understand the process and findings, which may help better inform product development programs underway outside of the Precert Program. At the same time, we can expect that the FDA will receive public commentary aimed at improving its development of screening criteria within the Precert Program. We look forward to watching the progress of this innovative approach to the regulation of software.

NEWS ANALYSIS

FDA Guidance offers clarity on manufacturer data sharing

The U.S. Food and Drug Administration ('FDA') published on 30 October 2017 the final version of its guidance, 'Manufacturers Sharing Patient-Specific Information from Medical Devices with Patients Upon Request' ('Guidance'), clarifying that the FDA's requirements do not prevent manufacturers of medical devices which store inputs from healthcare providers regarding a patient's status and ongoing treatment, or that record information about usage, alarms or outputs, from sharing patient-specific data recorded by the device with the patient diagnosed by or being treated with that device. "This is a circumstance in which the FDA is clarifying a question on which it has not previously provided guidance. The purpose of the Guidance is to facilitate sharing of data with patients when that is requested by the patient, but only if the manufacturer already has access to the information and does not need to alter the device in order to obtain the requested information," explains Yarmela Pavlovic, Partner at Hogan Lovells.

The FDA launched a consultation on a draft version of the Guidance in June 2016, following earlier reports about patients having difficulty when trying to get hold of data from medical devices, with some manufacturers concerned that to provide such information would need approval from the FDA. "The sharing of this data can potentially extend relationships with patients because manufacturers can provide patients with pertinent information about their health along with the devices," comment Cori Annapolen Goldberg, Partner, Krishna Kavi, Associate, and Rob Kantrowitz, Law Clerk, of Norton Rose Fulbright US LLP.

The manufacturer is under no obligation to provide data and whether it does so will be an internal decision. "In some cases, patient specific information may not be useful without having a medical professional interpret the information," said David M. Hoffmeister, Partner at Wilson Sonsini Goodrich & Rosati. "Furthermore, patient data collected by a medical device does not cover an analytical report that may be prepared by the manufacturer and provided to the healthcare professional for interpretation, e.g., a report analysing aggregate data from a heart monitor." "Many manufacturers may not have access to patient data," adds Pavlovic. "For example, many mobile applications with data stored on the cloud are designed such that data are encrypted except when viewed by authorised users. If the manufacturer does not already have a right to access the data, the Guidance is clear that they should not make changes only to provide the requested data. In addition, there are instances in which the company may have access to data that feeds into a final output for the user. The FDA makes clear in the Guidance that it is not intended to permit disclosure of these data unless they are part of the intended output of the device."

According to FDA Commissioner Scott Gottlieb, M.D., the Guidance is a step towards "[encouraging] transparency through greater access to health information." However, "Manufacturers should be wary not to cross the lines of diagnosing or evaluating the patient-specific information when they provide it to the patients, as that role should be left to providers," note Goldberg, Kavi, and Kantrowitz. "It is also important to note that the FDA does not intend this Guidance to change privacy protections in place through HIPAA and the associated HIPAA Privacy Rule."