FDA Regulation of AI in SaMD

A law firm can only be as good as the opportunities presented by its clients. Epstein Becker Green ("EBG") is fortunate to have had the opportunity to work with companies developing artificial intelligence ("AI") for almost 10 years, and the firm has advised more than 60 startups bringing AI to health care in ways that the media has identified as "cutting edge."

We represent companies in all manner of Food and Drug Administration ("FDA") compliance, although most typically these days we're involved with developing a strategy for premarket clearance or approval. But this FDA AI practice is in the context of EBG's broader FDA practice in which we routinely handle all regulatory issues, both premarket and postmarket.

Policy Work in Digital Health

EBG over the last decade helped define the regulatory requirements applicable to software that employs AI in the diagnosis or treatment of patients. Our experience is the product of having clients that are leading the way.

We have represented the following four coalitions or associations in the FDA software policymaking process:

1) mHealth Regulatory Coalition ("MRC") | 2010 to 2015 | FDA Regulation of Mobile Health

Prior to 2013, FDA offered very little guidance on when and how companies involved in mobile health were regulated. For the MRC, the following three FDA guidances were the direct result of EBG's advocacy:

- Mobile Medical Apps, September, 2013
- Wellness Products, January 2015
- Accessories to a Medical Device, January 2015

2) CDS Coalition | 2012 to Present | FDA Regulation of Clinical Decision Support Software

On behalf of the coalition, EBG spent a couple of years developing a model for differentiating regulated and unregulated clinical decision support software, partly on the basis of whether the software is designed to be transparent. "Transparency" means that the user can see through the software to view the underlying data on which recommendations are based, and understand the clinical logic the software is applying.

EBG's advocacy directly led to two policy developments:

- Section 3060 of the 21st Century Cures Act, which codified the transparency concept, enacted in December 2016
- FDA's proposed guidance on clinical decision support software, December 2017

In 2018, EBG, on behalf of the CDS Coalition, commented on the proposed guidance for clinical decision support software, recommending that FDA (1) layer in the International Medical Device Regulators Forum (or "IMDRF") risk framework and exempt low-risk clinical decision support software, (2) remove language inconsistent with the statute that would prevent software based on machine learning from ever being exempt, and (3) then re-proposing the guidance. FDA adopted all three recommendations.

EBG also drafted, on behalf of the CDS Coalition, industry guidelines for achieving transparency in clinical decision support software.

Professional Activities

Beyond representing coalitions, EBG is also professionally engaged in the advancement of regulatory improvements through volunteer activities. For example, one of our attorneys is actively involved in helping to develop so-called "Good Machine Learning Practices" under the sponsorship of Xavier University. The use of machine learning in the pharmaceutical and medical device industries bears the risks of unanticipated outcomes, unintended (and undetected) degradation in time, confusion for users, and incompatibility of results with other software that may use the output of the evolving algorithm. Good Machine Learning Practices will support the ability of organizations to use AI in a responsible and effective way.

3) AI Startups in Health Coalition ("AISHC") | 2019 to Present | FDA Regulation of AI in Software as a Medical Device

Organized by EBG, more than 1,000 entrepreneurs signed up for the spring 2019 Startup Roadshow at universities across the country to learn about FDA regulation of AI in health care. One of the outcomes of those meetings was the realization that startups need a stronger voice in FDA policy making regarding the agency's new approach to regulating AI. Consequently, EBG launched AISHC.

AISHC will focus on two FDA initiatives:

- Software Precertification Pilot Program: Version 1.0 Working Model, January 2019
- Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) – Discussion Paper and Request for Feedback, April 2, 2019

The goal of this coalition will be to ensure that FDA's new programs properly take into consideration the unique concerns of AI startups.

4) Continua Health Alliance ("Continua") | 2008 to 2015 | Interoperability and Connected Health

Continua is a founding member of the Personal Connected Health Alliance ("PCHA"). The PCHA is an international nonprofit organization established by Continua, mHealth Summit, and HIMSS to represent the consumer voice in personal connected health.

EBG has served as regulatory counsel to Continua. Continua is dedicated to the development of its Design Guidelines, which include global industry standards to ensure end-to-end, plug-and-play interoperability of personal connected health devices for the seamless and secure collection, transmission, and storage of personal health data. With Continua, EBG helped organize a summit meeting with FDA as well as ongoing discussions regarding how to achieve interoperability.

Individual Company Experience

EBG got an early start in guiding companies developing AI applications in health care. Almost 10 years ago, EBG began representing some of the biggest names in this area developing products.

EBG takes very seriously its obligation to protect confidences revealed to it. In this area, much of what EBG is presently doing involves helping companies developing AI products that are not yet public, such as:

- Several applications of AI fundamentally changing the process of interpreting radiological images
- AI apps that will fundamentally change how primary care is provided
- The use of AI in virtual reality to deliver care to patients with mental health conditions
- Software that employs digital assistants to help manage health care of aging patients living at home
- AI applications that help hospitals and other care providers remotely monitor those patients they discharge
- AI applications that guide people through physical therapy
- AI applications that guide women in family planning
- AI applications that employ cognitive behavioral therapy to help people cope with chronic conditions such as diabetes
- AI applications that analyze hospital medical records to find patients who are at risk of certain diseases or conditions
- AI applications in dermatology

Unfortunately, the above list is quite cryptic, but it reflects in some measure the literally dozens of AI applications in health care in which EBG is helping companies chart their paths through FDA. As already observed, EBG represents more than 50 companies working on the cutting edge of AI applications in health care.

In all this work, EBG attorneys work closely with EBG Advisors consultants who bring special expertise needed to understand the complexities of these products. Our consultants include one with a PhD in machine learning with substantial experience at FDA, as well as a consultant with a master's degree in electrical engineering who is well versed in preparing premarket submissions addressing machine learning applications.

FDA Regulation of AI Used in Software with Pharmaceuticals

EBG also has a special niche within this area focusing on software that is used in tandem with pharmaceutical products. This practice area came about because for more than 15 years, EBG has had a special focus on the so-called “combination products,” products that combine, for example, regulated drugs and medical devices. So, digital products for pharmaceutical use was a natural extension that began, for the firm, about 10 years ago.

Policy Work: Combination Product Coalition | 2003 to Present | FDA Regulation of Combination Products

The Combination Products Coalition is comprised of companies in the drug, medical device, and biologics industries that make combination products. Over the years, the coalition has evolved to have a special focus on drug-led combination products.

The coalition’s work is quite broad, involving all regulatory areas of interest to combination products, but one of the working groups focuses on digital health. That group has been actively working now for several years to provide FDA with input on the need of the industry for clarity with regard to requirements applicable to drug-led combination products that involve software.

Individual Company Work

As before, we cannot be too specific about the exact products on which we are engaged. But at a high level, they include for both large pharmaceutical companies as well as innovative software companies, the following clinical areas:

- Software that scours a hospital’s electronic health record to identify patients who are trending negatively and who may need drug intervention
- Software that helps tailor drug dosages for individual patients
- Software that supplements a drug by helping patients break their addiction
- Software that helps guide patients through lifestyle changes that also improve the effectiveness of a drug

Wellness and Other Software Unregulated by FDA

Over the last several years, wellness and other software unregulated by FDA has been one of our biggest practice areas. Not surprisingly, many companies want to avoid FDA regulation if there's a way to do so that is both legal and meets their business objectives. We help guide companies away from FDA regulation through careful management of both the design process and the process of defining the intended use for the product and associated marketing materials.

Policy Work

EBG represents the mHealth Regulatory Coalition, which is responsible for pressing FDA for guidance on wellness products.

Framework

We listen to our clients. Carefully. And when a client explains its technology and its business and marketing goals, we often end up discussing with it the categories of technology that FDA does not regulate, in case the company would prefer to begin in unregulated space and perhaps later develop a product for the regulated space. We often suggest that it is easier to learn to crawl, then to walk, and finally to run.

Four Lawful Ways to Avoid FDA Regulation—or at Least Required Clearance or Approval—in the Digital Health Space

1. Not a medical device
    a. Requires analysis of true intended use
2. Low-risk devices that at least do not require clearance or approval—and, in some cases, even less
    a. Class I devices that do not require clearance or approval
    b. Enforcement discretion expressed in FDA guidance, which can include what might otherwise be a class I or even a class II medical device
    c. Statutorily exempt low-risk devices, such as administrative, Medical Device Data Systems, and electronic health records
3. Wellness devices
    a. This is a blend of statutory exemption (narrower) and enforcement discretion through the wellness guidance (broader)
    b. Must be low risk
    c. Can mention a disease or condition if
        i. Stated appropriately as the product of wellness
        ii. "Generally recognized" evidence to support connection between wellness intervention and disease or condition
4. Clinical decision support software that is transparent, as specified by 21st Century Cures statute
    a. Gating requirements:
        i. Not intended to acquire, process, or analyze a medical image or a signal
        ii. Intended for the purpose of displaying or analyzing medical information
        iii. Intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition
    b. Risk overlay: FDA applies enforcement discretion to software that merely informs clinical decision-making, without driving or guiding it, for nonserious diseases or conditions where the software is directed at health care provider, regardless of transparency
    c. FDA says it will apply the same logic to patient directed software: There are two significant limitations, however:
        i. The information needs to be understandable to a patient, rather than a health care provider; FDA policy puts "understandable to a patient" at somewhere around the fifth-grade level
        ii. This only applies to the lowest-level risk—again, software that merely informs clinical decision-making, without driving or guiding it, for nonserious diseases or conditions

We go through these options with a client to identify whether any of them might best fit the client's business objectives at this particular stage in the company's development. This requires not only careful listening on our part, but also creative strategy—thinking outside what might be the client's predefined box.

Individual Product Experience

We have gone through this analysis with clients dozens of times for technologies such as low-impact physical therapy, weight management, sleep management, mental acuity and attention, and so forth. This work is frequently done in tandem with data collected through sensors either on the body or someplace else.

Learn more at https://www.ebglaw.com/artificial-intelligence/.